

PHARMACEUTICAL COMPOUNDING: PROPOSED LEGISLATIVE SOLUTION

HEARING OF THE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS UNITED STATES SENATE ONE HUNDRED THIRTEENTH CONGRESS FIRST SESSION ON EXAMINING PHARMACEUTICAL COMPOUNDING, FOCUSING ON A PROPOSED LEGISLATIVE SOLUTION

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PHARMACEUTICAL COMPOUNDING: PROPOSED LEGISLATIVE SOLUTION

THURSDAY, MAY 9, 2013

U.S. SENATE,
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
Washington, DC.

The committee met, pursuant to notice, at 10:12 a.m., in room SD-430, Dirksen Senate Office Building, Hon. Tom Harkin, chairman of the committee, presiding.

Present: Senators Harkin, Alexander, Mikulski, Casey, Franken, Baldwin, Murphy, Warren, Enzi, and Roberts.

OPENING STATEMENT OF SENATOR HARKIN

The CHAIRMAN. Good morning. The Senate HELP Committee will come to order. I'm sorry for being late. I have excuses, but I won't use them.

Last November, this committee convened a hearing to better understand what caused one of the worst public health crises this country has experienced in recent years, the meningitis outbreak that has claimed the lives of 53 Americans and sickened over 700. Through that hearing and the efforts of our investigation teams, we have developed a better understanding of the legal and regulatory gaps that allowed owners and managers at the New England Compounding Center to disregard basic procedures to ensure that the products they were manufacturing were sterile. This gross negligence had heartbreaking consequences for families nationwide.

Following that hearing, members of this committee initiated a bipartisan investigation involving all of our offices. We met several times a week to identify and examine the various issues around compounding and to conduct discussions with stakeholders with a goal of developing a draft proposal.

Today, we have convened this hearing to look forward. We want to talk about solutions. As most of you know, almost 2 weeks ago, we released a bipartisan draft proposal designed to improve the safety of compounded human and animal drugs. Our purpose today is to gather key stakeholder input about that draft so that we can refine it as we move toward markup.

As we talk to our witnesses today, I will be asking them how well the draft fulfills the purposes which we want it to, to make clear the compounding oversight responsibilities of State and Federal authorities; second, to provide FDA the tools it needs to oversee the entities for which it will be primarily responsible. And, again, we want to see how well our bill does fulfill those respon-

sibilities. Does it really give FDA the tools it needs? Does it clarify responsibilities? Does it improve the safety of compounded drugs so that patients nationwide can trust the quality and safety of their medicines?

So with what we learn today, we will then proceed to modify and improve the draft as necessary with the goal of a markup before Memorial Day. So I look forward to working again, as we have in the past, with members of this committee to refine our draft to better ensure the quality of compounded drugs.

With that, I'll yield to Senator Alexander.

OPENING STATEMENT OF SENATOR ALEXANDER

Senator ALEXANDER. Thanks, Mr. Chairman. Thanks to you and to Senator Roberts, Senator Franken, and other Senators and the staff, all those who have worked on this. This has been a good process. The outbreak of fungal meningitis was a nightmare for Tennesseans. We've had 150 cases with 15 deaths. There was some heroism on the part of some of our State officials who discovered the problem, helped alert other States about it, and worked with the FDA.

When we met to discuss this in November, I made it clear that I have a single goal here, or at least a primary goal. That is to make sure who is on the flagpole, who is accountable, to eliminate any confusion about responsibility.

Let me take just a minute on that. When I was a new Governor, I remember a cabinet meeting, and we had a very important bill to pass. We all agreed we'd go to work on it, and we passed it during the week in the legislature. We got back together a week later and nothing had happened. So I said, "Let's try something else."

Granville Hinton was a member of the cabinet, and I said, "Granny's on the flagpole, so we'll all help him, but if it passes, it's to his credit, and if it doesn't, it's his fault." And you'd be surprised. We got back together the following week, and it had passed because Granville knew that.

That happens in a lot of lines of work. Hyman Rickover understood it with the nuclear Navy in the 1950s. He told the captains of every nuclear submarine—he personally hired them, and he told them they had two responsibilities. One was the ship, and the second was the reactor, that if anything went wrong with the reactor, the captain was personally responsible for it, and his career in the Navy was probably in the dust if anything happened.

As a result, during that entire time since the 1950s, there's never been a death as a result of a nuclear reactor on a Naval submarine. I'd like to see that kind of accountability here when we talk about pharmacies. We've developed a bill, working with FDA, pharmacists, doctors, hospitals, and very many members of this committee, that passes that test, that tries to set clear lines for who is in charge and when they're in charge. I hope to hear from the witnesses today what they think about this and how we can improve it.

To very briefly summarize it, it creates three categories. One is the traditional drug manufacturer. FDA would continue to regulate that. The second category is a new category defined as compound manufacturers. These are businesses that make sterile products in

advance of a prescription and sell them across State lines. They fill a need when the products made by the drug manufacturers need to be tailored or combined for certain hospital patients. Hospitals increasingly turn to compounding manufacturers to make those changes to the drugs. This new category of compounding manufacturers will be regulated by the FDA.

The third category is the traditional pharmacy, defined as pharmacies that sell compound non-sterile products, such as lotions, that only sell in their State or receive prescriptions before beginning the compounding. States will continue to oversee and regulate these traditional pharmacies. So when you walk into a facility, it will be clear who is in charge of regulating that facility, or if in the draft regulation it's not, we would like your advice about how to make it clear.

We heard a lot in our discussions, some that we expected to hear, some more than we expected. For example, we heard more than we expected to hear, I think, about drug shortages. We have tried to address that, and we know that compounded products are not the answer to drug shortages. But we don't want drug shortages, and we want to deal with that, and we can.

There are a number of other suggestions that we heard that we tried to incorporate. We can deal with that in the questions of several Senators who want to be involved. So, Mr. Chairman, I'd like to submit my entire statement for the record and let us proceed with the hearing.

[The prepared statement of Senator Alexander follows:]

PREPARED STATEMENT OF SENATOR ALEXANDER

Thank you, Mr. Chairman. I'm very glad to be here and to be having this important hearing.

The ongoing outbreak of fungal infections stemming from contaminated product from the New England Compounding Center has been a nightmare for Tennessee. As of May 6, there have been 741 cases of fungal infections, including 55 deaths. Tennessee has seen over 150 cases and 15 deaths.

When we met to discuss this tragedy last November, I made it clear that my goal was to work on crafting legislation that would clarify who is in charge and on the flagpole for regulating compounding facilities. I wanted to ensure that something like last year's outbreak never happens again—to make sure we can walk into any one of our 60,000 drugstores or pharmacies, or go to our doctors or pain clinics, and not have to worry about whether the medicines we get there are safe.

For the past several months Senator Harkin and I, along with Senator Roberts and Senator Franken and all of the Senators on the committee, have been working together on this draft legislation. I truly believe we have developed a bill that sets clear lines for who is in charge of what and when.

With input from the Food and Drug Administration (FDA), State boards of pharmacy, pharmacists, doctors, hospitals, consumer groups, and others, we have developed a system to define three different categories of facilities and to make it clear who regulates the businesses in each one.

The first category is drug manufacturers. The FDA would continue to regulate traditional drug manufacturers and approve their drugs for safety and efficacy before being marketed.

The second category is a new one, defined as “compounding manufacturers” in our draft legislation. These are businesses that make sterile products in advance of a prescription and sell them across State lines. These compounding manufacturers fill a need when the products made by drug manufacturers need to be tailored or combined for specific hospital patients. Hospitals increasingly turn to compounding manufacturers to make those modifications to the drugs. In our draft legislation, this new category of compounding manufacturers will be regulated by the FDA. Compounding manufacturers will register and list their products with the FDA, and be inspected by the FDA. Compounding manufacturers will also have to investigate and report when things go wrong.

The third category is the traditional pharmacy, defined as pharmacies that compound non-sterile products (such as lotions), or only sell in their State, or receive prescriptions before beginning the compounding. States will continue to oversee and regulate these traditional pharmacies. State boards of pharmacy will have clear guidance on which facilities to license as a pharmacy.

If, during an inspection, the State board realizes that a pharmacy business has grown and started shipping sterile products out of State and does not have prescriptions for those products, the State board of pharmacy will know that facility should be under FDA jurisdiction and not licensed as a pharmacy. The goal is that when you walk into a facility, it will be clear who is in charge of regulating that facility.

We are making clear distinctions between these businesses to enable clear regulation of each one. This means that businesses currently operating in the first and third categories will have to make a change. For example, a facility that currently sells only a few sterile products without a prescription across State lines will have to decide whether to upgrade that facility and meet FDA requirements, or change their business model to get prescriptions before compounding. This is necessary to ensure that consumers and doctors know that the products they are using are safe.

Our bill also mandates increased communication between States and the FDA. We know that a lack of communication was a major factor in the case with NECC. Many States sent red flags about NECC to FDA, but we do not know if the Massachusetts Board of Pharmacy received those same complaints. The FDA assumed that the Massachusetts Board of Pharmacy was in charge, and the State board assumed that the FDA was in charge. Under our proposal, if the FDA receives a complaint from a State board about an out-of-state traditional pharmacy, the FDA has to notify the State board where the facility is located of the complaint within 15 days.

I know that some people advocate for allowing the FDA to have access to records of all pharmacies, but I believe that would blur the lines of accountability when the purpose of this bill is to clarify accountability. If States and the FDA can communicate effectively, there is no need for duplicative inspections. I hope to hear ideas from both the FDA and the National Association of the Boards of

Pharmacy today about how to improve coordination and communication in our proposal.

Throughout the process of writing this legislation, we heard about the impact drug shortages are having on patient care. We want to ensure that nothing we're doing makes drug shortages worse. Continued access to patient specific compounded products is very important, and we need to do all we can to alleviate current shortages of manufactured drugs.

Compounded products are not the answer to drug shortages. We would prefer for patients to receive drugs approved by the FDA and manufactured in a FDA facility. However, in the case of drug shortages where no other manufacturer can step in and there is not an option to import products, patients and providers need access to compounded products.

We received over 100 comments on this draft last week, so I understand there are ways to improve and clarify the proposal. We want to work with stakeholders to improve the bill. One provision that I look forward to discussing is the ability of the FDA to designate product categories and bulk materials as not suitable for compounding. We received comments that this authority undermines State regulation of traditional pharmacy, and I want to make sure that we clarify how and when these authorities can be used.

Tennessee recently passed a law allowing office use of certain compounded products. I do not want this bill to change how Tennessee chooses to regulate its traditional compounding pharmacies. I look forward to discussing how the authorities for the FDA would complement the State approaches, how to improve State and FDA coordination, and some other provisions with our first witness, Janet Woodcock from the FDA. I also want to thank her for all the time her staff has put into this discussion. If they had been on top of it a year ago we may not be in this situation, but I'm glad the Agency is working with us now.

We received lots of comments on how hospitals should be treated under this proposal, and I look forward to a good discussion with Dr. Kasey Thompson on our second panel on how to ensure quality products in every care setting.

Last, I want to thank everyone who took the time last week to comment and read the bill. I believe we all share the same goal that each patient should be able to access the product prescribed by his or her doctor, and have assurance that the product is made to a suitable quality standard. To ensure safe compounding and manufacturing practices, we must be clear about who is accountable for regulating those practices.

The CHAIRMAN. Thank you, Senator Alexander.

Senator Mikulski has to recuse herself as the chair of the Appropriations Committee. She has to go and work to get our allocations and get our appropriations bills in line. And since she's been so much involved in this effort, and so much of this takes place in her State with the FDA and others, I yield to Senator Mikulski.

STATEMENT OF SENATOR MIKULSKI

Senator MIKULSKI. Just a few quick words, Mr. Chairman. Thank you. I'm not recusing myself. I'm excusing myself. Recuse acts like I'm a party to the bad part of the situation.

[Laughter.]

Let's not parse recuse, excuse. The fact is there's no excuse if we don't act on this legislation. And I'd like to compliment you, Mr. Chairman, and Senator Alexander for the bipartisan way that you've led this committee to come up with this solution.

It is, indeed, a dire problem. My own State was affected—26 confirmed cases, three deaths. The Maryland General Assembly acted, but as our Commissioner of Health and Governor said, a State solution requires a national solution. I'm going to continue to work with you, because we need prevention, which will be the legislative framework. We need enforcement, which is how we make sure FDA is funded to do the job with the kind of accountability that you and Senator Alexander talk about.

I will be excusing myself so we can work to begin to get our appropriations allocations done so the subcommittees can do their work. So forward together. I'll leave at the conclusion of Dr. Woodcock's testimony.

The CHAIRMAN. Thank you, Senator. You're excused but never recused. I got that.

Apart from the normal procedure—usually, the procedure of this committee is always Chair and Ranking Member. But because this basically is his bill and it's one that he's been involved in for so long, I'm going to ask the indulgence of the committee to recognize for 5 minutes or so the Senator from Kansas, Senator Roberts.

STATEMENT OF SENATOR ROBERTS

Senator ROBERTS. Well, thank you, Mr. Chairman. First, let me say that I've never known the distinguished Senator from Maryland to recuse herself from anything. I affectionately call the Senator Princess Leia. On occasion, she calls me Luke. But she is a Jedi Knight, and she will go do her very best in her role on the Appropriations Committee.

Mr. Chairman, I just have a very brief opening statement, and then during the questioning, if you would grant me some extra time to clear up some misinformation on this bill that's out there—unfortunately, the same folks that were active to prohibit our efforts to address the compounding issue in 2002 and 2007 are back at it again.

And I think that's most unfortunate, and I want everyone listening, everyone here in this committee room—and I know all of my colleagues know this—to know that our legislation does not prohibit access to lifesaving medication and therapies for patients. And it does everything, everything, to ensure an open and transparent process to make sure that doesn't happen.

I know every member on this committee wants more transparency with regards to any bill and a process to make sure that that doesn't happen. I would yield back my time at this point. When we have time for questions, there are several myths I would like to clear up with what I think is factual information. All wit-

nesses and all those present, there will be a test after my comments and after we adjourn, and the penalty for not understanding this will be to go to Dodge City where you'll be hung by the neck until you are dead.

[Laughter.]

The CHAIRMAN. All right. Proceeding on——

[Laughter.]

The CHAIRMAN [continuing]. Our first witness is Dr. Janet Woodcock, Director of the FDA's Center for Drug Evaluation and Research, called CDER. Under Dr. Woodcock's direction, CDER evaluates and monitors the safety and effectiveness of drugs, helps provide doctors and patients with the information they need to make wise decisions about medication use and takes action against products that are unapproved, contaminated, or fraudulent.

Dr. Woodcock joined the FDA in 1986 and previously served as FDA's Deputy Commissioner and Chief Medical Officer. She has led many of FDA's drug initiatives such as the introduction of risk management to drug safety and the modernization of drug manufacturing. Dr. Woodcock testified at our hearing earlier last year.

We welcome you back again, Dr. Woodcock. Your statement will be made a part of the record in its entirety. Please proceed as you desire.

STATEMENT OF JANET WOODCOCK, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, SILVER SPRING, MD

Dr. WOODCOCK. Thank you, Mr. Chairman, Ranking Member, and members of the committee. We're here because of an appalling tragedy that resulted from tainted medicine that was given to unsuspecting patients. It's unbelievable that this happened in the 21st century. This tragedy was only the worst in a series of outbreaks involving compounded products over the past decade, a large series of outbreaks.

In retrospect, FDA, we think, should have been more aggressive in applying our existing authorities to this industry, in spite of the ambiguous statute and multiple challenges by industry. We are being more aggressive now. We're inspecting pharmacies that we know about that we think pose the highest risk, and we're seeing serious quality issues at these pharmacies.

Even in the light of recent events, some of these firms are actually challenging our authority, delaying or denying full access to their records. Twice, we've had to get administrative warrants from the courts and have U.S. marshals accompany our inspectors in order to get into the facilities. We've had to threaten warrants in other cases to get cooperation from these facilities.

Just because we're inspecting doesn't mean we will succeed in getting them to comply. Lack of clarity in our statutory authorities is not the only concern. The current legal framework is the wrong fit for this industry, which has evolved and grown tremendously over the past 12 years and really wouldn't be recognizable as a traditional pharmacist of, say, 25 years ago.

Make no mistake. I'm here to tell you that in the absence of changes, these tragedies will happen again. There is no doubt of

this. Since the NECC outbreak, we have found fungal organisms in additional compounded products, some of which were about to be given to patients and were only stopped by alert health personnel before they were actually administered to cancer patients. That's why the work you're doing to draft legislation is so critically important. We must have changes or this is going to happen again.

The draft the committee released last week would give us really important new oversight tools that would better protect the public. For the very highest risk products, the ones implicated in most of these outbreaks, it would require Federal registration so we know who the compounders are, where they are, and what they're making. It would require compliance with Federal quality standards and require reporting to FDA of serious adverse events so we can act before these potential problems really get out of hand.

It would provide us with clear authority to inspect records and would require clear labeling of compounded drugs to allow prescribers and consumers to make more informed choices. In fact, we've heard from prescribers. They had no idea where these drugs really were coming from and that there might be additional risks.

For all compounders, it would allow us to prohibit compounding of the most complex, high-risk drug products and to restrict the starting materials that could be used to those that are known to have high quality. We also appreciate that the draft would provide funding to help defray the cost to us of these additional oversight activities.

We are concerned, however, about a couple of things. As currently drafted, the bill might blur the line between a compounding manufacturer and a conventional manufacturer. Those conventional manufacturers' products must undergo FDA review and approval before marketing, and this could create incentives on the other side for those types of firms to try to slip into being considered a compounding manufacturer.

In addition, the discussion draft does not provide us clear access to records of all firms engaged in compounding. This is critical to our effectively investigating outbreaks and also determining whether a firm is posing as a traditional compounder or actually is a compounding manufacturer, and to determine whether traditional compounders are violating any other Federal requirements that the discussion draft places on all compounders, including prohibition of compounding of certain drugs that are very risky.

So let me reiterate the importance of the bill that you're working on and the importance of your efforts. If, in fact, action is not taken, this will happen again. It's really not a matter of whether. It's a matter of when. So we want to keep working with you. We really commend you. This bill is a huge step in the right direction, and we hope that our testimony will help clarify any existing issues.

Thank you.

[The prepared statement of Dr. Woodcock follows:]

PREPARED STATEMENT OF JANET WOODCOCK, M.D.

INTRODUCTION

Mr. Chairman and members of the committee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research at the Food and Drug Administra-

tion (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss important issues related to pharmacy compounding. We appreciate the leadership this committee has shown in drafting legislation to try to address the limitations and ambiguities in current law.

We are at a critical point where we must work together to improve the safety of drugs produced by compounding pharmacies. As the compounding industry has grown and changed, we have seen too many injuries and deaths over many years caused by unsafe practices. Dr. Margaret Hamburg, Commissioner of Food and Drugs, testified in front of this committee on November 15, 2012, soon after the emergence of a tragic fungal meningitis outbreak associated with compounded methylprednisolone acetate (MPA), a steroid injectable product distributed by the New England Compounding Center (NECC). To date, that outbreak has been associated with 55 deaths and over 740 people sickened in 20 States. Sadly, NECC was not an isolated incident. Indeed, over the past 20 years we have seen multiple situations where compounded products have caused deaths and serious injuries. For example:

- In 1997, two patients were hospitalized with serious infections after administration of contaminated riboflavin injection prepared by a Colorado pharmacy.
- In 2001, 13 patients in California were hospitalized and 22 received medical care following injections from contaminated vials of a steroid solution. Three patients died as a result.
- In 2002, five patients in North Carolina suffered from fungal meningitis resulting from contaminated methylprednisolone acetate made by a South Carolina pharmacy. One person died.
- In 2005, contaminated cardioplegia solution, made by a firm located in Maryland, resulted in five cases of severe system inflammatory infections; three of these patients died. In 2007, three people died from multiple organ failure after a Texas compounding sold superpotent colchicine that was as much as 640 percent the labeled strength.
- In 2010, FDA investigated a cluster of *Streptococcus endophthalmitis* bacterial eye infections in patients who received injections of Avastin repackaged by a pharmacy in Tennessee.
- In 2011, there were 19 cases of *Serratia marcescens* bacterial infections, including nine deaths, associated with contaminated total parenteral nutrition products.
- In 2012, 43 patients developed fungal eye infections from contaminated sterile ophthalmic drug products. At least 29 of these patients suffered vision loss.
- Recently, in 2013, FDA investigated reports of five cases of eye infections in patients who received Avastin repackaged by a pharmacy in Georgia. The Avastin was contaminated with bacteria.

These incidents are emblematic of long-standing issues associated with the practice of compounding and the public health concerns that can result from unsafe practices in compounding pharmacies.

Since the NECC outbreak, nine additional firms have voluntarily recalled sterile compounded or repackaged drug products through FDA as of May 6, 2013. In one very recent incident, the presence of floating particles, later identified to be a fungus, was reported in five bags of magnesium sulfate intravenous solution, resulting in a nationwide recall of all sterile drug products produced by the pharmacy (over 100 products). Fortunately, we have not received reports of patient injury from these products. In another recent recall, all sterile drug products (approximately 60 products) from a second pharmacy were recalled as a result of reports that five patients were diagnosed with serious eye infections associated with the use of repackaged Avastin. Moreover, we believe that presently, there are hundreds of other firms operating as compounding pharmacies, producing what should be sterile products and shipping across State lines in advance of or without a prescription. However, the current legal framework does not provide FDA with the tools needed to identify and adequately regulate these pharmacies to prevent product contamination.

The history of this issue shows that there is a need for appropriate and effective oversight of this evolving industry. It is clear that the industry and the health care system have evolved and outgrown the law, and FDA's ability to take action against compounding that exceeds the bounds of traditional pharmacy compounding and poses risks to patients has been hampered by limitations and ambiguities in the law, which have led to legal challenges to FDA's authority to inspect pharmacies and take appropriate enforcement actions.

The fungal meningitis outbreak has caused the Agency to review our past practices with regard to our oversight of compounding pharmacies, and has led to some preliminary conclusions.

In my view, even in the face of litigation and continuous challenges by industry to our authorities, we can nonetheless be more aggressive in pursuing enforcement actions against compounding pharmacies within our current limited authority. I can assure you that we are being more aggressive now. We have established an agency-wide steering committee to oversee and coordinate our efforts, and we have taken several important steps to identify and inspect high-risk pharmacies that are known to have engaged in production of sterile drug products.

Using a risk-based model, we identified 29 firms for priority inspections focused on their sterile processing practices. During these 29 inspections, in two instances, FDA identified secondary firms associated with the priority inspections, for a total of 31 firms. We have taken investigators who would normally be doing inspections of conventional drug manufacturers and assigned them to conduct inspections of those pharmacies whose history suggests a greater risk of potential quality issues with their compounded products. We have coordinated our inspections with State officials, who have accompanied our investigators in most cases. At the same time, we have also continued to conduct for-cause inspections, often at the request of our State counterparts who invited us to accompany them on the inspections. Since the fall, FDA has conducted 26 for-cause inspections in addition to the 31 described above. When we identified problems during any of the inspections, at the close of the inspection, we issued an FDA Form 483¹ listing our inspection observations. We have issued an FDA-483 at the close of 47 of the 57 inspections we have conducted since last fall. We have seen some serious issues, including quality concerns that have led to product recalls. Observations have included: lack of appropriate air filtration systems, insufficient microbiological testing, and other practices that create risk of contamination.

Notably, even in light of recent events, and even though we are often working with the State inspectors, our investigators' efforts are being delayed because they are denied full access to records at some of the facilities they are inspecting. Just during the recent inspections, several pharmacies delayed or refused FDA access to records, and FDA had to seek administrative warrants in two cases. And although we have been able to eventually conduct the inspections and collect the records that we have sought, our ability to take effective regulatory action to obtain lasting corrective action with regard to substandard sterility practices remains to be seen.

As we have noted in the past, our ability to take action against inappropriate compounding practices has been hampered by ambiguities regarding FDA's enforcement authority, legal challenges, and adverse court decisions, and we have learned that the law is not well-suited to effectively regulate this evolving industry. For example, hospitals have come to rely on compounding pharmacies that function as "outsourcers" producing sterile drugs previously made by hospital in-house pharmacies. If FDA brings charges against a pharmacy, alleging that it is manufacturing a "new drug" that cannot be marketed without an approved application, the pharmacy will have to either obtain individual patient-specific prescriptions for all of its products or stop distributing the products until it obtains approved new drug applications for them, something most outsourcers are unlikely to do. Several of the pharmacies FDA inspected are some of the largest outsourcers in the country. These pharmacies supply large numbers of sterile drugs produced in relatively large quantities to hospitals nationwide, and a shut-down at these firms is likely to cause disruptions in the supply of drugs to hospitals and other health care providers. FDA should have more tailored authorities appropriate for this type of compounding pharmacy.

In the Commissioner's last appearance before this committee, she presented a framework that could serve as a basis for the development of a risk-based program to better protect the public health, improve accountability, and provide more appropriate and stronger tools for overseeing this evolving industry. We have since met with over 50 stakeholder groups, including pharmacy, medical, hospital, payer, and consumer groups, and State regulators, to help further our understanding and inform our framework. Today, I will first provide background on FDA's current legal authority over compounded drugs, then provide additional details about the framework, and suggest specific actions that Congress can take to help us better do our job and prevent future tragedies like this one.

¹A form FDA-483 is issued when investigators observe any significant objectionable conditions. It does not constitute a final Agency determination of whether any condition is in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or any of our relevant regulations, but the observations often serve as evidence of a violation of the FD&C Act and its implementing regulations.

FDA'S LEGAL AUTHORITY OVER COMPOUNDED DRUGS

FDA regards traditional pharmacy compounding as the combining or altering of ingredients by a licensed pharmacist, in response to a licensed practitioner's prescription for an individual patient, which produces a medication tailored to that patient's special medical needs. In its simplest form, traditional compounding may involve reformulating a drug, for example, by removing a dye or preservative in response to a patient allergy. It may also involve making an alternative dosage form such as a suspension or suppository for a child or elderly patient who has difficulty swallowing a tablet. FDA believes that pharmacists engaging in traditional compounding provide a valuable medical service that is an important component of our health care system. However, by the early 1990s, some pharmacies had begun producing drugs beyond what had historically been done within traditional compounding.

After receiving reports of adverse events associated with compounded medications, FDA became concerned about the lack of a policy statement on what constituted appropriate pharmacy compounding. In March 1992, the Agency issued a Compliance Policy Guide (CPG), section 7132.16 (later renumbered as 460.200) to delineate FDA's enforcement policy on pharmacy compounding. It described certain factors that the Agency would consider in its regulatory approach to pharmacies that were producing drugs.

The compounding industry objected to this approach and several bills were introduced, some with significant support, to limit the Agency's oversight of compounding.² In November 1997, S. 830, the Food and Drug Administration Modernization Act of 1997 (FDAMA), was signed into law as Public Law 105-115.³ FDAMA added section 503A to the FD&C Act, to address FDA's authority over compounded drugs.⁴ Section 503A exempts compounded drugs from three critical provisions of the FD&C Act: the premarket approval requirement for "new drugs"; the requirement that a drug be made in compliance with current good manufacturing practice (cGMP) standards; and the requirement that the drug bear adequate directions for use, provided certain conditions are met. These provisions were the subject of subsequent court challenges, which have produced conflicting case law and amplified the perceived limitations and ambiguity associated with FDA's enforcement authority over compounding pharmacies. In 2002, immediately after a Supreme Court ruling that invalidated the advertising provisions of section 503A, FDA issued a revised compliance policy guide on compounding human drugs. Several additional legal challenges and court decisions then followed. More recently, FDA made significant progress toward issuing another CPG. In fact, FDA was on track to publish a revised draft CPG in the fall of 2012, but the fungal meningitis outbreak intervened and we are now reevaluating the draft. It is important to note, however, that a CPG is not binding on industry and updating the CPG would not alleviate all issues with section 503A.

A look at FDA's attempts to address compounding over the last 20 years shows numerous approaches that were derailed by constant challenges to the law. As a result, presently, it is unclear where in the country section 503A is in effect, and section 503A itself includes several provisions that have impeded FDA's ability to effectively regulate pharmacy compounding practices including those relating to prescription orders, medical need, and copying FDA-approved products.

Apart from section 503A, there are additional provisions in the statute that have impeded effective pharmacy compounding regulation. For example, if certain criteria are met, the FD&C Act exempts compounding pharmacies from registration and the obligation to permit access to records during an inspection. As a result, FDA has limited knowledge of pharmacy compounders and compounding practices and limited ability to oversee their activities.

LOOKING AHEAD

The Administration is committed to working with Congress to address the threat to public health from limitations in authorities for effective oversight of certain

²H.R. 5256, Pharmacy Compounding Preservation Act of 1994, introduced Oct. 7, 1994, 1 co-sponsor; H.R. 598, Pharmacy Compounding Preservation Act of 1994, introduced Jan. 20, 1995, 141 cosponsors; H.R. 3199, Drug and Biological Products Reform Act of 1996, introduced March 29, 1996, 205 cosponsors; H.R. 1060, Pharmacy Compounding Act, introduced March 13, 1997, 152 cosponsors; H.R. 1411, Drug and Biological Products Modernization Act of 1997, introduced April 23, 1997, 16 co-sponsors.

³Public Law 105-115, FDAMA, 111 Stat. 2296 (Nov. 21, 1997), available at <http://www.gpo.gov/fdsys/pkg/PLAW-105publ115/pdf/PLAW-105publ115.pdf>.

⁴Id.

compounding practices. To that end, FDA has developed a framework that could serve as the basis for the development of a risk-based program to protect the public health.

RISK-BASED FRAMEWORK

Recognizing the history of compounding practice, FDA supports the long-standing policy that all compounding should be performed in a licensed pharmacy by a licensed pharmacist (or a licensed physician), and that there must be a medical need for the compounded drug.

Further, we believe there should be a distinction between two categories of compounding: traditional and non-traditional. Traditional compounding would include the combining, mixing, or altering of ingredients to create a customized medication for an individual patient with an individualized medical need for the compounded product, in response to a valid patient-specific prescription or order from a licensed practitioner documenting such medical need. Traditional compounding, while posing some risk, plays an important role in the health care system, and should remain the subject of State regulation of the practice of pharmacy.

Non-traditional compounding would include certain types of compounding for which there is a medical need, but that pose higher risks. FDA proposes working with Congress to define non-traditional compounding based on factors that make the product higher risk such as any sterile compounding in advance of or without receiving a prescription, where the drug is distributed out of the State in which it was produced. Non-traditional compounding would be subject to Federal standards adequate to ensure that the compounding could be performed without putting patients at undue risk, and FDA would inspect against and enforce these Federal standards. Such a definition focuses on the highest risk activities and offers a uniform degree of protection across all 50 States, for highest-risk compounding activities.

Non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. Sterile products produced in advance of or without a prescription and shipped interstate should be subject to the highest level of controls, established by FDA and appropriate to the activity, similar to cGMP standards applicable to conventional drug manufacturers.

In addition, FDA believes that with noted exceptions, certain products are not appropriate for compounding under any circumstances. These products would include: (1) what are essentially copies of FDA-approved drugs, absent a shortage justification based on the drug appearing on FDA's shortage list; and (2) complex dosage forms such as extended release products; transdermal patches; liposomal products; most biologics; and other products as designated by FDA. Producing complex dosage forms would require an approved application and compliance with cGMP standards, along with other requirements applicable to manufactured drug products.

FDA believes that there are other authorities that would be important to support this new regulatory paradigm. For example, FDA should have clear ability to collect and test samples of compounded drugs and to examine and collect records in a compounding pharmacy, just as the Agency does when inspecting other manufacturers. FDA should also have clear ability to examine records such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, to respond to public health threats, and to enforce Federal standards.

FDA also believes that an accurate inventory of pharmacies engaged in non-traditional compounding would facilitate appropriate oversight and coordination with State regulators. In addition, FDA looks forward to working with the Congress on potential improvements that may include label statements and adverse event reporting that have proven useful in other areas. A user-fee-funded regulatory program may be appropriate to support the inspections and other oversight activities outlined in this framework. We look forward to working with Congress to explore the appropriate funding mechanisms to support this work, which could include registration or other fees, as Congress has authorized and FDA has successfully implemented in other settings.

CONCLUSION

Given our experiences over the past 20 years and the recent fungal meningitis outbreak, we must do everything we can to clarify and strengthen FDA's authority in this area. We appreciate the bipartisan efforts of the committee to clarify the law regarding the oversight of compounding pharmacies and look forward to the oppor-

tunity to work with the committee to address remaining issues. Thank you for your leadership in taking this important first step.

I am happy to answer any questions you may have.

The CHAIRMAN. Thank you, Dr. Woodcock, and your suggestions are, believe me, under serious consideration. We'll take those into account as we refine and put this bill together. I think they're great suggestions, and, as I said, we've discussed those recently. Hopefully, we'll be able to incorporate those in the draft.

Let me just ask a few questions, and you touched on this. But just develop a little bit more about keeping traditional manufacturers from deciding to become a compounding manufacturer, because you said that might happen. What could we do to ensure against that?

Dr. WOODCOCK. We had advised that any compounding manufacturer would also have to hold a pharmacy license in the State in which they were located. And I understand the reason for not doing that was to make the flagpole clear.

However, the evolving industry is really doing pharmacy operations. To a great extent—and I'm sure you've heard from the hospitals—hospitals are outsourcing their pharmacy operations. Clinics, pain clinics, as well as many other clinics that maybe are now office buildings—they don't have a pharmacy located in their office building, so they buy these products from a pharmacy, right now a compounding pharmacy.

These are regular pharmacy operations, most of the operations that are being done. And I think having the State board oversee that, requiring that to be a pharmacy, clearly distinguishes that from a drug manufacturer that is an entity that really has to apply for an application for each—an NDA to market any given product. So there has to be a clear separation, we think.

Also, those personnel in the compounding manufacturers should have appropriate qualifications for pharmacy operations, which means pharmacists, pharmacy technicians. The States oversee much of that. They license pharmacists in their States.

The CHAIRMAN. Very good. Thank you. How important is it that this legislation be effective immediately upon enactment? If we pass this bill with, say, a transition period or a delayed effective date, would that compromise your current efforts at overseeing pharmacy compounding?

Dr. WOODCOCK. We feel there would have to be a delayed effective date. That would be the most appropriate. We could work on guidance for the industry, those who would be moving into the compounding manufacturing status, about what they would have to comply with.

The CHAIRMAN. So you're saying it shouldn't be effective immediately.

Dr. WOODCOCK. We think that would cause disruption if all of it were effective immediately. And we would be happy to work with you on how that could be set up.

The CHAIRMAN. If we delayed it, that would not compromise your efforts at overseeing?

Dr. WOODCOCK. We would continue to do what we're doing now, aggressively—

The CHAIRMAN. What we're doing now is not effective.

Dr. WOODCOCK. What we're doing now is—we would inspect and enforce standards for human safety, all right, according to our current statute. It is complicated, and I think we should work with you on this.

The CHAIRMAN. I'd like to work with you on that, because I'm not certain that we see eye to eye on this one. I just think that a delayed period creates a lot of problems, but we'll be glad to discuss that.

Let me ask you this. Does the draft provide the FDA the tools it needs, in terms of both authorities and resources, to oversee pharmaceutical compounding?

Dr. WOODCOCK. The user fee proposal that's in there, or the fee proposal, would probably provide about, we estimate, 60 percent of the resources that would be needed, and we really appreciate the committee putting that in. We recognize that right now, the resources to do this are primarily coming from our inspectors who inspect the traditional drug industry, both the generics and the innovator, and so, over the long term, that would decrease our effectiveness.

As far as the provisions, as I said, we would like to have broader records authority than what is put in the bill right now, because we feel we really need to get into pharmacies to make sure they're not posing as traditional pharmacies or they're not committing practices that are forbidden under the legislation.

But, particularly, if there's an outbreak, we have reports, and we go in, and they say, "No, you can't come into our pharmacy." And we need to find out who they've shipped to. We need to get samples and test them. And so not having the ability to look at their records and so forth could, in an outbreak, impede our ability to protect the public health.

The CHAIRMAN. That's an area that we're really going to have to look at, too, and that's accessibility of records.

My time is up. I'll turn to Senator Alexander.

Senator ALEXANDER. Thanks.

Dr. Woodcock, it seems to me the most important thing about this bill is the new category, compounding manufacturer. To me, clarity is what I'm—the flagpole is what I'm looking for. And a compounding manufacturer would be one that makes a sterile product in advance of a prescription and sells it across a State line. So if you do that, you're in that category. Right? Is that the way you understand it?

Dr. WOODCOCK. Yes.

Senator ALEXANDER. And then the compounding manufacturer would be inspected by and registered and list their products with the FDA.

Dr. WOODCOCK. That's correct.

Senator ALEXANDER. Now, what we're recommending—the draft recommendation—is that you be totally in charge of that facility, that you be on the flagpole for that facility. But your testimony suggests that the State have some role, too. Doesn't that just leave us where we are, which is confusion between what the State—can't you then say, "Well, the State should have done that," and they can say, "Well, I thought the FDA was doing it"?

Dr. WOODCOCK. No. We would take full responsibility. However, we feel that this is a pharmacy operation. It's almost like a Federal pharmacy operation. In some sense, it is a pharmacy operation, because what would keep a traditional manufacturer—if they don't have to be a pharmacy, then they can say they're a compounding pharmacy and begin to make perhaps unapproved drugs.

So the rationale for this third category is really that these are pharmacies that are doing operations that are beyond the scope of ordinary pharmacy practice—

Senator ALEXANDER. Right.

Dr. WOODCOCK [continuing]. And really need Federal intervention. But they still are pharmacies. They're still doing pharmacy operations.

Senator ALEXANDER. Well, the bill requires that they have a licensed State pharmacist in there.

Dr. WOODCOCK. Yes.

Senator ALEXANDER. But why shouldn't—I mean, that's confusing to me. It seems to me that it's important for a facility to know that if I make a sterile product in advance of a prescription and I sell it across the State line, I've got one regulator, and that regulator is the FDA, period. And then the doctor knows that, the customer knows that, the patient knows that—everybody knows, and the FDA knows that, that it's your job to make sure that place is safe.

Dr. WOODCOCK. And we agree that we would take full responsibility, that the registration and listing provisions that you've put in the bill enable us to know who those folks are and—

Senator ALEXANDER. But then why do you need to have the State involved?

Dr. WOODCOCK. Well, it's on the other side, like the people who are traditional manufacturers, which distinguishes this facility from any—

Senator ALEXANDER. Traditional manufacturers or pharmacists?

Dr. WOODCOCK. Traditional manufacturers. It's the other side. It's not the pharmacy that is—

Senator ALEXANDER. Well, you regulate traditional manufacturers.

Dr. WOODCOCK. We do. Well, I believe we could have more conversation about this. I understand—

Senator ALEXANDER. I just think—to me, it's very important. I mean, I think Admiral Rickover was onto something, and we could probably apply it in a lot more aspects of the Federal Government. Just in my human experience, I've discovered that if it's absolutely clear who's on the flagpole, who's in charge, that reduces the risk of failure, and it improves the chances of success. I'm more comfortable with your being in charge of compounding manufacturers, just like you are with traditional manufacturers, so there's no confusion.

If I could ask one other question, the draft bill includes an exemption to the compounding manufacturer category for interstate shipments within a hospital system. Now, could you comment on why you believe interstate shipments of sterile products within hospital systems don't pose the same public health risks as other compounders?

Dr. WOODCOCK. They pose certain risks, and, certainly, intra-state shipment of sterile products and sterile products that are used intra-state alone pose certain risks. And, certainly, non-sterile products have caused deaths. So making medicines and shipping them around is not without risk. We've tried to pick the highest risk category, which is where a manufacturer not associated with taking care of the patients is manufacturing sterile products and shipping them all around to other entities.

Senator ALEXANDER. But why would—

Dr. WOODCOCK. A hospital system is already in charge of their patients, and they may wish to centralize their pharmacy operations. But if they had a pharmacy operation, say, in one State, within that hospital system, they would be doing that and giving it to their own patients. So they already have responsibilities for the care and safety of their patients within their hospital system.

Senator ALEXANDER. What if they contract that out? What if the hospital system contracts that out?

Dr. WOODCOCK. If they contract it out, then it's to a different entity, and if that entity is shipping intra-state, then that is a compounding manufacturer.

Senator ALEXANDER. If they contract it out, it becomes outside the exemption, and they're regulated by the FDA.

Dr. WOODCOCK. That is correct, and that is what much of these operations are. They're outsourcing operations that once occurred in the hospital pharmacy to sort of—

Senator ALEXANDER. But if Vanderbilt Hospital has its own—

Dr. WOODCOCK. Hospital pharmacy.

Senator ALEXANDER [continuing]. Hospital pharmacy, then all the parts of the Vanderbilt Hospital is exempt from this.

Dr. WOODCOCK. That's correct.

Senator ALEXANDER. If it contracts it out to the Harkin, Incorporated, then Harkin or Alexander are regulated by the FDA.

Dr. WOODCOCK. That's how we understand the current proposal, and that's what we would agree with.

The CHAIRMAN. I hope we make that clear in our draft. Thank you very much.

In order, I have Senator Warren, Senator Roberts, Senator Mikulski—no, she's not—Senator Enzi, Senator Murphy, Senator Baldwin.

Senator Warren.

STATEMENT OF SENATOR WARREN

Senator WARREN. Thank you, Mr. Chairman. As the senior Senator from Massachusetts, I feel a special duty to ensure that we do everything possible to protect people from unsafe drugs. Massachusetts was home to the New England Compounding Center, the compounding pharmacy that was responsible for the fungal meningitis outbreaks that killed 53 people and made 733 people sick. This outbreak was in part the result of longstanding failures in government regulation at both the State and Federal levels, a lack of coordination between State and Federal oversight, and a lack of clarity in the existing regulations.

This unregulated industry is not a Massachusetts problem. It is a national problem. The current state of our oversight of the

compounding industry is outdated and inadequate. And as the data make clear, it represents a continuing threat to public health. I take this threat seriously. Those drugs can go anywhere, and a patient has no way to assess the safety of the pills that a pharmacist hands out or the drugs that a doctor injects into a patient.

People count on us to put laws in place that will protect our citizens from this sort of harm. This is one of the most basic functions of regulation. I think a lot of members of this committee recognize that. I'm very pleased that Democrats and Republicans on this committee have been able to come together over the last several months to develop this draft legislation. I'm pleased because we all agree that a tragedy like this should not happen again, that it can be prevented, and it's our job to prevent it.

So the question I want to understand—I want to get a little transparency behind this—is exactly the scope of the problem that we're dealing with. We've all concentrated on the New England Compounding Center, and we should. It attracts our attention. But can you tell the committee, Dr. Woodcock, how many patients have been harmed by injury, by infection, or by death since 1997, when Congress first acted to prevent harms associated with compounding?

Dr. WOODCOCK. Certainly. I think the real problem is we don't know. Pew in their testimony today has a chart of known outbreaks and known deaths going back over a decade, and also other problems such as blindness, severe injuries, and so forth from compounded products. But because we don't have an inventory or identification of these firms, and it's difficult sometimes to detect the harm at an individual level, we actually don't know.

What we do know is that many of these practices that we have uncovered cannot assure sterility of the sterile products. I'd like to read from a recent hearing that New Jersey had, all right?

Senator WARREN. Go ahead, Dr. Woodcock.

Dr. WOODCOCK. This was from Dr. David Newton, who is an expert and a pharmacy professor, and he was chair of the Sterile Compounding Committee of USP numerous times. What he said was the following. He said that the statistical likelihood of contamination in a medium-risk sterile compounding environment is approximately 1 percent. That's 1 in 100.

Now, that's tolerable if you're in the basement of the hospital in the pharmacy there, and you send it right up to the floor, or you're making it up right beside the patient, and you inject it right in the patient. But if these are made in mass quantities, and 1 percent of them may be contaminated, statistically, and they are shipped all around, and they're put in inventory, and they're sitting, this allows organisms to grow, and that's kind of the root cause of this problem.

We have grown multiple organisms out of samples we have taken when we've done these inspections of compounding pharmacies.

Senator WARREN. Dr. Woodcock, I just want to push on a point. I very much appreciate that what you're identifying is that there are some really bad practices out there, and the assumption is that those bad practices are causing illness, injury, and possibly even death.

The question I wanted to know the answer to is how much, and you've told me you don't know. Why don't you know? You're the Federal Drug Administration. Why don't you know how many people have been killed from these drugs?

Dr. WOODCOCK. There is no requirement right now for registration and listing, which would be telling us who they are, where they are, and what they're making.

Senator WARREN. So no one has to tell you.

Dr. WOODCOCK. No.

Senator WARREN. What happens when you ask?

Dr. WOODCOCK. Sometimes we can't get their records, particularly their shipping records, and so doing investigations can be difficult or impeded by refusal to allow us access.

Senator WARREN. So we're here today because of one tragedy that became public. We don't know how many other people have been made sick. We don't know how many other people have died.

Dr. WOODCOCK. We know there have been multiple other outbreaks and multiple other episodes of fatalities from compounded products.

Senator WARREN. But, basically, the compounding industry doesn't tell, and as long as they don't tell, we don't have the kind of public scrutiny that causes us to move forward with this kind of legislation.

Thank you, Dr. Woodcock. I just want to say I think it's unconscionable that we have failed to regulate this industry for so long and put the public at risk. I'm very much committed to working with you and with everyone on this committee to make sure that we put a stop to this.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you, Senator Warren.

Senator Roberts.

Senator ROBERTS. Thank you, Mr. Chairman, and my colleagues, and with your indulgence, I might go a little over time with what I hope is a factual response to some misinformation that I think is out there. I would remind the committee that way back in 2002–3, we had a pharmacist in Kansas City, MO, who was diluting cancer drugs and selling them as if they were fully potent. That was exposed with the help of the Kansas City Star, by the way, and a young man named Mark Morris.

He's in prison now, and he's serving time, and that was one of the reasons I got into this some 10 years ago. Lately, as the Senator from Massachusetts has indicated, we've had this tragedy with 53 deaths and 700 illnesses. If anything, that really galvanized the committee, and I appreciate everybody's participation and leadership.

To address some specific information now being circulated, Myth No. 1: Under the proposal, traditional compounders would be subject to current good manufacturing practices—that's called cGMP. That's the acronym—the quality standards that apply to pharmaceutical manufacturers.

Fact: Traditional compounders are exempt from cGMP requirements. The draft exempts traditional compounders from the cGMP requirements—read section 501(a)(2)(B); adequate directions for use, section 502(f)(1); and the new drug-approval requirement, sec-

tion 505 for human drugs and section 512 for animal new drug approvals. See page 5, lines 12 to 22.

I think, everybody, if you wanted to write that down, we can certainly give that to you and proceed from there.

Myth No. 2: The proposal prohibits the use of liposomal or transdermal products.

This draft does not ban the compounding of any specific products. The proposal does direct the FDA to establish a list of products, however, that are too complex to currently be compounded. But that list will be developed through an open transparent regulatory process with input from stakeholders.

I realize this kind of process may represent an endangered species in the overall regulatory process of the Federal Government. But with this committee, we're going to conduct oversight and make sure that that happens.

Myth No. 3: The proposal creates loopholes for pharmaceutical companies to manufacture new drugs without new drug applications, i.e., the NDAs.

Fact: Under current law, compounded drugs are considered new drugs. As is true with all new drugs, the new drug application requirements apply unless an entity meets the criteria to be either a traditional compounder or a compounding manufacturer. Under the proposal, neither a traditional compounder nor a compounding manufacturer can make a product from a book unknown to USP—that's the book that all the pharmacists use—or FDA and distribute it in an interstate commerce without an investigational new drug exemption, NDA or ANDA.

Myth No. 4: The proposal creates a loophole for hospital compounding pharmacies that will allow them to compound outside of industry best practices.

Fact: Hospital-based pharmacies are treated as traditional compounders under the proposal. They are subject to the same restrictions as other traditional compounders. Hospital-based compounding will continue under the exact same State Pharmacy Board, Joint Commission, and Center for Medicare and Medicaid Services standards that exist today.

Myth No. 5: By categorizing all compounded drugs as new drugs, the burden will be so great that it is impractical to compound even to fill a specific prescription.

Fact: Under current law, FDA already categorizes all compounded drugs as new drugs, and this proposal affirms that principle. The proposal exempts traditional compounders from the new drug approval requirements, cGMP standards, and adequate directions for use requirements so they are not subject to the major requirements applicable to most new drugs. Similarly, compounding manufacturers are exempt from the new drug approval requirements and the adequate directions for use requirements.

Myth No. 6: The proposal prohibits traditional compounders near State lines to ship products interstate because of arbitrary boundaries.

Fact: The traditional compounders can ship non-sterile products across State lines without receiving a prescription before compounding the product or ship any product, sterile or non-sterile,

across State lines if they receive a prescription before compounding.

Myth No. 7: The proposal will make drug shortages worse.

Fact: The proposal allows for compounding of products on the FDA drug shortage list.

Myth No. 8: The proposed limits eliminates doctors' options to prescribe the most beneficial treatment, in their medical opinion, for a patient.

Fact: The day of enactment, FDA is directed to create a list of products too complex to compound. Only after a transparent and regulatory process, again, with a comment period for the public and doctors, can FDA add any product to that list.

Finally, Myth No. 9: The proposal eliminates drug compounding for animals.

Fact: The exemptions from new drug requirements for traditional compounders and compounding manufacturers apply to drugs compounded for humans and animals. The proposal allows compounding of animal drugs from FDA-approved products or from bulk chemicals subject to restrictions. Any FDA-approved product for either humans or animals can be compounded to treat the animal, except for drugs on the do-not-compound list established by the FDA.

In addition, the FDA will establish a list of bulk chemicals that can be used to compound a drug for major species and food for animals while any bulk that meets USP standards can be used for minor species.

I hope this clears up some misinformation that's been out there, Mr. Chairman. I thank you for your indulgence. I'll have additional questions for the panel.

The CHAIRMAN. I want to thank you, Senator Roberts, for reading that list. I've had that before. My staff has informed me that over 2,000 e-mails have come in to Senators' offices. One Senator—I don't know that I need to mention his name—said that he alone got over 200 e-mails basically propounding all of these myths, that that was going to happen.

So the same forces, as I say to my good friend from Kansas, that sunk your bill in 2007 are back out there again. So I appreciate your highlighting the myths and the facts that are in this bill. I thank you for that.

Senator Enzi.

STATEMENT OF SENATOR ENZI

Senator ENZI. Thank you, Mr. Chairman. The more I hear about this, the more confused I get. I thought that the FDA, the CDC, and the HMS has a pretty good system of locating things when they went awry. In fact, I remember a spinach outbreak that we had, and the three of them showed unusual—no, I think as we investigated, it was usual cooperation. And with as few as 20 cases spread over three States, they were able to isolate that there was a problem, and they were able to trace it back to the farm where it happened.

I don't understand how this one got so far out of hand before anything was discovered. But, at any rate, you're reaching into a whole area here that boards of pharmacies, which are State-based,

have been operating on. Obviously, there was a breakdown in it, and if you say these other cases happened, there's been a breakdown in that, too.

But that's kind of the people on the flagpole right now, those State boards of pharmacy. And they're supposed to go into these records, and they ought to have the ability to let you know if somebody is a manufacturer. But it doesn't seem like we need to expand the FDA operation in order to do what is already supposed to be done by the States.

There are a lot of things that we give out primacy for. OSHA is one of them, and that saves the Federal Government having a lot of inspectors. But the Federal Government is very inefficient. They seem to be able to do about three inspections a month, and at that rate, it would take 500 years for them to get around to all the businesses. And I could see where, if we keep expanding FDA, we can run into that same kind of a problem.

I do think these things need to be reported faster. I think that we ought to make sure that the people in the States are trained well to be able to tell whether it's a manufacturing facility or whether they're doing their normal thing. And pharmacists checking on pharmacists—I don't think we have enough pharmacists in the whole United States.

But could you clarify whether the FDA believes that under the draft bill, the compounding manufacturers should follow good manufacturing procedures, GMPs, or whether the FDA intends to establish new standards more appropriate for the scope and scale of their operations?

Dr. WOODCOCK. We would intend if the bill is passed to establish specific requirements, similar to what we've done for positron emission tomography, where that's a very specialized area, and we've put forth specific requirements. Those drugs have to be made with a cyclotron because they're radioactive. We put forth very specific requirements, and that industry is operating under those requirements. We would hope to tailor, again, specific requirements to the issues raised by sterile compounding.

Senator ENZI. And those aren't just GMPs?

Dr. WOODCOCK. GMPs have a very broad range of scope of all parts of drug manufacturing. For example, manufacturing compounders would not be doing drug synthesis or making new drugs sort of from scratch, which is what the generic and innovator industry does.

Senator ENZI. So we're going to have a new regulatory regime for large-scale drug compounders and establish new restrictions on what traditional pharmacists can and cannot compound. This new framework will require rulemaking, then. I think you just said that. The pharmacists in my State have commented that they hope the FDA will communicate any new requirements to them in a user-friendly manner. What Senator Roberts read wasn't hardly user-friendly to me, but maybe it is to a pharmacist.

Can you commit that the FDA will provide an open and transparent process for this rulemaking associated with the bill? And can you provide your thoughts on how we can make everyone aware of the products on the do-not-compound list?

Dr. WOODCOCK. Yes. We will have extensive public discussion and comments. We would propose to put out interim guidance on things so that people would understand. We work with the National Board of Pharmacies as well as with the States and the State Board of Pharmacies so that we can get out to the professional societies, and we can work with all the different associations of pharmacists. So we have many ways to get the word out.

I can't stress enough, though, that the industry we're talking about regulating here with the Federal Government is not traditional compounding as people would have thought of it, say, 20 years ago. It is very large scale and is not in response to individual prescriptions.

We have long recognized at FDA the value of pharmacy compounding and the way it can tailor medications to different unmet medical needs. However, this industry has changed and grown up, so this is a new type of practice that has evolved. And it raises the stakes on risk, because they're doing large-scale, sterile processing of drugs.

And as I read earlier, the way it is being done now and the standards that apply, there is a finite chance of contamination. We've seen this contamination happen again and again and again. And this industry is not required to not only identify themselves to us, but submit adverse event reports if anything goes wrong. So we don't have a good way with this new industry, this evolving industry, of finding out what's going on with it.

Senator ENZI. It seems like if we have a requirement for vitamin manufacturers to report adverse events——

Dr. WOODCOCK. We do.

Senator ENZI [continuing]. That we certainly ought to do it for almost everything. I've used my time up. Sorry.

The CHAIRMAN. Let's see. Senator Murphy is not here.

Senator Baldwin.

STATEMENT OF SENATOR BALDWIN

Senator BALDWIN. Thank you, Mr. Chairman and Ranking Member. I appreciate the fact that you're holding this hearing, and I want to thank you, in particular, for managing a very open process. I know that this committee has been working on this issue for many, many months now, even before I joined this committee, and that individuals on this committee have been working on this issue for many years, and I appreciate that work. There's a very encouraging sense of an open and collaborative process, and everyone has seemed welcome at the table.

Last year's tragic meningitis outbreak underscored the importance of updating Federal compounding policy. And at the same time, compounded drugs are an important part of patient care. For some patients, these specially tailored drugs are the only medicines that can work effectively. It's critical that patients continue to have access to these treatments, but it is also important to make sure that the compounded drugs that people count on are safe, and that our regulatory system does not allow bad actors to exploit loopholes and jeopardize patient safety.

I believe this bipartisan draft proposal represents significant progress toward striking the right balance between patient safety

and patient access to compounded treatments. And I look forward to the process that we're going to undertake as we move this forward.

Dr. Woodcock, I really appreciate you sharing your expertise on this subject with us. The draft proposal appropriately focuses FDA regulation on large entities that compound the riskiest products. It also includes minimum standards for all compounding practices to help ensure patient safety when somebody gets a customized drug from their neighborhood pharmacy.

The proposal would require pharmacists to use recognized chemical ingredients to compound a drug and allows the FDA to publish a list of ingredients that may not be used for compounding. I wonder if you can explain why it would be necessary to restrict the use of some chemical bulk ingredients. And, in particular, can you discuss how the FDA would determine what goes on that list?

Dr. WOODCOCK. Certainly. There are a variety of risks that can be introduced that these provisions are directed at. First, the bulk ingredients are generally made overseas in India or China. If they have not been subject to FDA inspection, if they're simply purchased, say, from some supplier, they may not be what they purport to be, or they may be contaminated with chemicals or other impurities.

Second, for some of the very complex dosage forms that we have, for example, certain patches that release drugs, even the innovator manufacturers have trouble making these. And sometimes they will dump drugs into circulation and you could die, because you have an extended release patch on, and maybe it gets a little warm, or you have a lot of covers on, and they haven't made it properly, and the warmth causes all the drug to go into your circulation, and you get a massive overdose.

There's some very, very—and we work with our manufacturers to try and deal—we had another one where if people took a drink of alcohol, it would dissolve the extended release mechanism, and the whole thing would release into the blood stream all at once, and people would get serious side effects. So the more complex the dosage form, the more difficult it is to manufacture.

Then we have another category which is—we're seeing this in dietary supplements now, where drugs we've taken off the market because they're too dangerous have been introduced into dietary supplements. And those types of drugs that actually have been removed for safety, we wouldn't want to be compounded and have our population exposed.

Senator BALDWIN. Because I have such limited time, let me just ask that this list, as you put it together, is compiled for safety purposes only and not for other reasons. And if that is the fact, what sort of procedural safeguards will be in place while you're developing this list to ensure that any restricted bulk ingredients are, in fact, dangerous or pose some safety risk to patients—

Dr. WOODCOCK. We certainly would have safety as our principal objective here.

Senator BALDWIN. Any other objectives?

Dr. WOODCOCK. Safety. That's really the primary objective.

Senator BALDWIN. There's anecdotal information, at least, that there will be folks who will be interested in that list for competitive

purposes and competitive advantage, and I want to make sure the FDA won't be manipulated in that way.

Dr. WOODCOCK. That's fair. In my world, there's always issues of competitive advantage, and we try to stick strictly to our objectives.

Senator BALDWIN. On a related issue, you highlighted the importance of prohibiting the compounding of copies of FDA-marketed approved drugs except for during drug shortages. I'm concerned about patient access when the approved drug is not available for reasons other than a shortage.

As one example, I think about a compound called 17-P, which was brought to market by a drug company at prohibitively high prices. This is a drug used to prevent preterm birth. And as a result, the compounded version of the drug is the only available option for many women. What tools does the FDA have or need to allow patient access to needed medicines in unique circumstances like this other than drug shortages?

Dr. WOODCOCK. The FDA really doesn't usually balance human safety considerations against economic considerations. This proposed statute, though, is attempting to make sure that there isn't widespread compounding of generic drugs and that generic drug firms simply enter the market without pre-market requirements, without going to the FDA and having bioequivalence testing and having their product approved and proper labeling, and simply marketing their drugs as compounded drugs, so that there's a big loophole that allows those drugs to enter the market and compete with the established industry and undermine the Federal process for introducing generic drugs into the market. That's the reason for those provisions.

The CHAIRMAN. Thank you, Senator Baldwin.
Senator Franken.

STATEMENT OF SENATOR FRANKEN

Senator FRANKEN. Chairman Harkin, Ranking Member Alexander, thank you for convening this important hearing and for all your work on pharmacy compounding in the wake of the meningitis outbreak last fall. You've led a transparent, as Senator Baldwin said, and productive process on an extremely complex issue. Thank you both for your leadership.

If my child or my wife urgently needed medicine, I'd ask many questions. Will my loved one get well? What's going to happen? But I should never have to ask the question whether the medicine that my family is given is safe or whether it is actually what the doctor said it should be.

But more than 1,000 patients and their families across Minnesota had to ask that question last year, because the contaminated medicine that they received could have caused enormous harm. More than 50 patients across the country died from these contaminated injections produced by a large-scale compounding pharmacy in Massachusetts that was essentially an unregulated drug manufacturer.

I come from Minnesota where we specialize in medical innovation. We have some of the best doctors and healthcare systems and biomedical pioneers anywhere in the world. Our Nation has an incredible capacity for innovation and development in this field.

There is no possible justification for allowing more than 17,000 vials of contaminated medicine to be shipped to providers throughout our country.

That's why my colleagues and I have worked so hard over the past several months to make sure that this never happens again. And I'll be the first to say that the draft we released 2 weeks ago isn't perfect, and that's why we asked for stakeholder comments, and that's why we're working very hard to update the draft based on the hundreds of pages of comments that we received. And I'd like to thank the many stakeholders who have worked productively with us to help improve our proposal.

Dr. Woodcock, there have been broad concerns among community pharmacists that our proposal would cause them to be regulated by the FDA and comply with manufacturer-level quality standards. Can you clarify whether traditional mom-and-pop pharmacies that do not compound batches of sterile products and ship them over State lines would have to change their current practices under this proposal?

Dr. WOODCOCK. They are left within the scope of traditional pharmacy compounding, and they would not be subject to the manufacturing rules of the FDA or many of the other provisions. Some of the do-not-compound issues that we've been talking about would apply, and that is a safeguard that actually has been in place to some extent over the years anyway. So, no, the traditional pharmacy compounding will not substantively change.

Senator FRANKEN. Dr. Woodcock, if our draft were to pass into law, do you believe that FDA would have the authority to prevent another company from behaving in the same manner as the New England Compounding Center did before the meningitis outbreak?

Dr. WOODCOCK. Firms shipping sterile products intra-state without receipt of a prescription, which would be the case for these large-scale shipments, would be subject to Federal registration, would be required under the law to register and list with the FDA. We would inspect them, and we would make sure they were complying with the proper accepted practices so that these drugs would be sterile.

Senator FRANKEN. Thank you. Dr. Woodcock, our draft gives the FDA the authority to produce a list of complex drugs that should not be compounded. I'll note that in the process of producing this list the FDA is required to go through the full notice and comment rulemaking process, which means that the FDA must get input from pharmacists and other experts on their proposal before it goes final.

Can you tell us if you believe that this list is important, and, if so, why?

Dr. WOODCOCK. Yes, I believe it's very important. I believe the scope of traditional pharmacy compounding is extremely important to patients, to practitioners. But it's also important that that remain safe, and that it not stray into areas where the risk is very high. That's why we're addressing the interstate shipment of sterile products.

But we're also addressing very risky practices where the risk would be too high. I think that is also very important. However, the goal is to not impede the traditional compounding practices.

Senator FRANKEN. Thank you, Dr. Woodcock. Thank you for your testimony, and my time is expired.

Thank you both, Mr. Chairman and Senator Alexander.

The CHAIRMAN. Thank you, Senator Franken.

Dr. Woodcock, thank you very, very much again for your testimony. I'm sure we'll have some followup questions perhaps in writing to submit to you. But thanks for your input on this as we continue to refine this draft.

Dr. WOODCOCK. Thank you, and we're delighted to work with you.

The CHAIRMAN. Thanks, Dr. Woodcock.

Now we'll call our second panel. First is Mr. Carmen Catizone, who is the executive director of the National Association of Boards of Pharmacy. They assist the State boards of pharmacy in protecting the public health, aids in interstate licensing, and helps develop competency standards for the practice of pharmacy.

Previously, Mr. Catizone was a president of the National Pharmacy Manpower Project of the National Conference of Pharmaceutical Organizations, as well as a past member of the U.S. Pharmacopeia Board of Directors.

Allan Coukell is here, the director of Medical Programs in The Pew Health Group, a division of the Pew Charitable Trusts. Mr. Coukell oversees initiatives related to medical products and services, including Pew's Drug Safety Project. In February, Mr. Coukell's group helped to convene a summit to discuss pharmaceutical compounding which included representatives from health professional organizations, compounding pharmacies, quality experts, and the Center for Disease Control and Prevention as well as FDA.

We thank you for doing that.

Mr. Coukell is both a pharmacist and a consumer advocate, and we welcome his perspective today.

Next is David Miller, executive vice president and CEO of the International Academy of Compounding Pharmacists, an association which represents pharmacists who focus on pharmaceutical compounding. Previously, Mr. Miller served as the executive director of the Maryland Pharmacists Association and the director of Pharmacy Affairs at Merck. Mr. Miller also testified at our hearing last November.

We welcome you back again, Mr. Miller.

Dr. Kasey Thompson currently serves as the vice president of the Office of Policy, Planning, and Communications at the American Society of Health-System Pharmacists, an organization which advises its members on the responsible use of compounded medications. Dr. Thompson has extensive knowledge regarding the safe use of compounded drugs, as he previously served as the American Society of Health-System Pharmacists' Director of the Center of Patient Safety. Dr. Thompson was also part of our panel in November.

We welcome you back again, Dr. Thompson.

As before, all of your statements will be made a part of the record. We ask that you summarize those in 5 minutes, and we'll move ahead to questioning.

First, we'll start with Mr. Catizone.

Thank you for being here and please proceed.

STATEMENT OF CARMEN S. CATIZONE, M.S., RPh, DPh, EXECUTIVE DIRECTOR, NATIONAL ASSOCIATION OF BOARDS OF PHARMACY, MOUNT PROSPECT, IL

Mr. CATIZONE. Thank you, Senator. Good morning, Chairman Harkin, Ranking Member Alexander, and committee members. I represent the State agencies, the State boards of pharmacy, that regulate pharmacists, pharmacies, technicians, and traditional compounding.

In regard to the Chairman's questions earlier, is the legislation effective, does it clarify the differences, does it address the needs of the States? The answer to all those questions is yes. We agree with the FDA that the situation can and will happen again. It's not a question of whether.

But some things have changed since the last hearing and since the unfortunate incident. One, the FDA has stepped up their inspections. That has made a significant difference to the landscape that existed prior to that time. It has also greatly assisted the State boards of pharmacy in trying to fulfill their mission to protect the public and regulate compounding.

Taking the lead from the Chairman's State of Iowa, we partnered with the Iowa Board of Pharmacy and to date have inspected 150 pharmacies across the United States in regard to compounding activities. Those inspections have involved not only the Iowa Board of Pharmacy, but the home State where that pharmacy is based. We will complete all 600 of Iowa's non-resident pharmacies before the end of 2013 and will have physically inspected those facilities with both our own trained staff as well as representatives from the Iowa Board of Pharmacy and the resident board of pharmacy as well.

We have also contracted recently with another State to inspect 150 of their in-state compounding pharmacies, and there are four other States that have pending legislation to recognize NABP to assist with the inspection of compounding pharmacies or to conduct those inspections on behalf of the State board of pharmacy.

The legislation presents and we support a clear distinction between compounding and manufacturing. The separation of compounding from manufacturing is critical to maintain the present authority of the States and address one of the contributing factors of the NECC crisis, specifically, what the FDA regulates and what the States regulate.

The provision in the proposed legislation that specifies a compounding manufacturer cannot be licensed as a pharmacy is essential to distinguishing from State-regulated compounding and FDA regulated manufacturing. If a compounding manufacturer is allowed to hold that dual licensure or registration, it will be more difficult to separate the two enterprises and could provide a veil for unscrupulous entities to obfuscate their activities.

NABP strongly supports the FDA receiving full and unlimited authority to access and seize any and all records related to the oversight and regulation of compounding manufacturers. We are concerned, however, that allowing the FDA access to pharmacy records for activities that are regulated by the States could create

a confusing situation, could take people off the flagpole, could change one of Senator Roberts' myths, could change the response to Senator Harkin's question about whether or not the FDA has authority over traditional compounding pharmacies.

We ask the committee to keep this provision intact and to help recognize and differentiate between compounding and manufacturing and State authority and Federal authority. The answer to remedy that situation is enhanced communication. We have built a database of electronic profiles for all pharmacies in the United States. We're including the inspection reports in those profiles and making that available real-time to States, and we'll make it available to the FDA and provide something to the public as well so they'll be able to search that database and decide whether or not they want to use that pharmacy for their services.

The other revision that we ask the committee to consider is the exemption of intra-state sterile compounding pharmacies, the intra-state. We believe that the same risks exist with intra-state compounding as with interstate. The operations that we've observed in intra-state are sometimes as large or larger than the interstate operations, and, therefore, we ask the committee to consider this provision and instead include the preparation of non-patient specific sterile prepared products for intra-state activities as a defining component of a compounding manufacturer and fall within the scope and authority of the FDA.

As stated earlier in our statement, the other provisions of the proposed legislation that address the safe preparation of medications and products for patients align well with the approaches suggested and requested by the States. The legislation proposed by the committee reflects the hard work conducted to understand a complex area of pharmacy practice, compounding, and a complex but necessary area of pharmacy practice to ensure that patients receive the appropriate medications.

But, most importantly, even though it is necessary and complex, compounding must be regulated effectively. The proposed legislation distinguishes between compounding and manufacturing, defines a new category of manufacturing that balances effective regulation with reality, and carefully constructs allowances and prohibitions on the scope and activities of a compounding manufacturer in order to meet patient needs while maintaining the necessary protections.

Thank you.

[The prepared statement of Mr. Catizone follows:]

PREPARED STATEMENT OF CARMEN S. CATIZONE, M.S., RPh, DPH

SUMMARY

On behalf of the State boards of pharmacy and NABP, I extend our appreciation to the committee for the proposed legislation that addresses the critical concerns identified by the States and validated by NABP through its inspections of compounding pharmacies. We welcome the clarifications provided by the proposed legislation to the regulatory uncertainties that currently exist—uncertainties that were a primary factor leading to the recent meningitis tragedy. Most importantly, the clarifications provide the needed distinction between compounding and manufacturing and provide a safe and equitable environment for both compounding and manufacturing to occur in the best interest of the patient.

AUTHORITY OF THE STATES

NABP supports a clear separation of “compounding manufacturer” from traditional pharmacy practice and compounding. The provision of the proposed legislation that specifies a compounding manufacturer cannot be licensed as a pharmacy is essential to distinguishing from State-regulated compounding and FDA regulated manufacturing. Our experience, and most recently our inspections of compounding pharmacies, affirms the importance of this prohibition in clarifying what activities fall under Federal jurisdiction and what entities can engage in compounding and operate under State jurisdiction.

TRANSITION PERIOD TO ENSURE UNINTERRUPTED PATIENT CARE AND
NECESSARY EXCEPTIONS

Equally tantamount to the recognition of State authority is the need to ensure an appropriate transition period with the States as well as to recognize exceptions for activities such as the preparation of radiopharmaceuticals. An appropriate transition period is needed so States will have sufficient time to alert pharmacists and other practitioners and ensure that patient care is continued and not halted by new requirements that may no longer allow certain activities that were previously permitted under State laws.

INTRA-STATE EXEMPTION FROM DEFINITION OF COMPOUNDING MANUFACTURER

NABP is concerned with the exemption for intra-state distribution of non-patient-specific sterile compounded products. It is our finding that non-patient-specific, sterile prepared products distributed intra-state bear the same risk levels to patients as products that are introduced into interstate commerce. In fact, some intra-state operations are as large or larger than interstate distributors of products and therefore the volume of products distributed, and the associated risk, can be equal to or greater than the interstate distribution of similar products. The differentiation between intra-state and interstate activities to define a compounding manufacturer could create patient safety concerns by unintentionally creating a safe haven for entities and individuals engaging in intra-state activities who have the intent to simply avoid the different and Federal-based requirements for interstate activities.

Good morning Chairman Harkin, Ranking Member Alexander, and committee members. I am Carmen Catizone, executive director of the National Association of Boards of Pharmacy (NABP). NABP thanks you for the opportunity to appear today and comment on the bipartisan *Draft Proposal on Pharmaceutical Compounding*. NABP commends the Senate HELP Committee for its diligence on this issue and the thoughtful approach taken in the draft proposal.

NABP is the impartial organization founded in 1904 whose members are the State agencies that regulate the practice of pharmacy. NABP supports the State boards of pharmacy by developing, implementing, and enforcing uniform standards for the purpose of protecting the public health. NABP also helps State boards of pharmacy to ensure the public's health and safety through its pharmacist license transfer, pharmacist competence assessment, and accreditation programs.

Following the tragic meningitis outbreak caused by contaminated injectable drugs, several States implemented compounding pharmacy inspections or conducted surveys of pharmacies, focusing especially on those engaged in sterile compounding. As part of the NABP Compounding Action Plan that was developed in November 2012 and implemented in December 2012, NABP partnered with the Iowa Board of Pharmacy and other States to begin conducting inspections of all nonresident pharmacies delivering compounded drugs into Iowa. Our initial inspections confirmed that what occurred at NECC was also occurring at other facilities in other States. To date, NABP has inspected approximately 150 pharmacies across the States and will continue our inspections until all of Iowa's approximately 600 non-resident pharmacies are inspected. In addition to the inspection program with Iowa, NABP recently executed an agreement with the State of New Jersey to assist with the inspection of in-state compounding pharmacies and the prosecution of any pharmacy or individual illegally engaged in the practice of compounding. Four other States have legislation pending or are in the process of designating NABP to conduct or assist with inspections of pharmacies for, or in their States.

The States thank the committee for the proposed legislation that addresses the critical concerns identified by the States and validated by NABP and its inspections of compounding pharmacies. As such, we welcome the clarifications provided by the proposed legislation to the regulatory uncertainties that currently exist and were

one of the primary factors leading to the recent meningitis tragedy. Most importantly, the clarifications provide the needed distinction between compounding and manufacturing and provide a safe and equitable environment for both compounding and manufacturing to occur in the best interest of the patient.

AUTHORITY OF THE STATES

NABP supports a clear separation of “compounding manufacturing” from traditional pharmacy practice and compounding. Although we would prefer that “compounding” not be included in the proposed designation because of the inference to traditional compounding and the confusion that could result, we understand that some terminology must be employed that describes the activity being regulated.

The separation of compounding from manufacturing is also critical to maintain the present authority of the States and address one of the contributing factors to the NECC crisis, ambiguous authority between the States and the Food and Drug Administration (FDA). The provision of the proposed legislation that specifies a compounding manufacturer cannot be licensed as a pharmacy is essential to distinguishing from State-regulated compounding and FDA-regulated manufacturing. Our experience, and most recently our inspections of compounding pharmacies, affirms the importance of this prohibition in clarifying what activities fall under Federal jurisdiction (FDA) and what entities can engage in compounding and operate under State jurisdiction (State boards of pharmacy).

If a compounding manufacturer is allowed to hold dual licensure/registration, it will be more difficult to separate the two enterprises and will provide a veil for unscrupulous entities to obfuscate their activities. NABP supports FDA receiving authority to access any and all documents and records required for the oversight and regulation of compounding manufacturers. We are concerned about allowing the FDA access to pharmacy records for activities that are regulated by the States. If an entity is manufacturing or compound manufacturing, then under the proposed legislation and current authority, the FDA will have access to all documents and records concerning these activities. Authorizing the FDA access to pharmacy records could create jurisdictional conflicts with the States and impede the States from investigating or prosecuting a case because the FDA has seized evidence or information needed by the State(s). What is needed in lieu of allowing such access is increased communication between the States and FDA.

NABP is collecting and maintaining data on the compounding pharmacies identified by the Iowa Board as well as those indicated by other boards of pharmacy. Our electronic data base of e-Profiles for pharmacies is being expanded and enriched to include all pharmacies licensed or registered in the United States by State boards of pharmacy and comparable State agencies. Data collected from the boards and the inspection reports provided by the States and through NABP’s activities with, or on behalf of the States, will be stored in an NABP Pharmacy e-Profile, allowing us to disseminate pertinent information among State boards and the FDA. States are now able to submit inspection reports and other related information to NABP for inclusion in pharmacies’ e-Profiles. The e-Profiles for Pharmacies will be made available at no cost to boards for use in making licensure and registration determinations for pharmacies, the FDA, and to the public for their use in selecting an appropriate pharmacy.

TRANSITION PERIOD TO ENSURE UNINTERRUPTED PATIENT CARE AND NECESSARY EXCEPTIONS

Equally tantamount to the recognition of State authority is the need to ensure an appropriate transition period with the States as well as to recognize exceptions for activities such as the preparation of radiopharmaceuticals. An appropriate transition period is needed so States will have sufficient time to alert pharmacists and other practitioners and ensure that patient care is continued and not halted by new requirements that may no longer allow certain activities that were previously permitted under State laws. One such example is the compounding “for office use” that is currently allowed in some States. It is our understanding that the proposed legislation addresses this concept in different provisions and that overall the classification of such activities is a State matter when the products prepared are distributed intra-state and a Federal matter when the products prepared are distributed in interstate commerce. If the proposed legislation is adopted and these distinctions are correct and implemented, States will need some time to make the adjustments in State laws in order to ensure uninterrupted patient care and close any regulatory gaps that might result.

INTRA-STATE EXEMPTION FROM DEFINITION OF COMPOUNDING MANUFACTURER

NABP is also concerned with the exemption of the intra-state distribution of non-patient-specific sterile compounded products. We support the logic of establishing a delineation point in order to more readily identify and regulate large-scale operations that conceivably pose more risk to patients than smaller operations. However, it is our finding that non-patient-specific, sterile prepared products distributed intra-state bear the same risk levels to patients as products that are introduced into interstate commerce. In fact, some intra-state operations are as large and larger than interstate distributors of products and therefore the volume of products distributed, and the associated risk, can be equal to or greater than the interstate distribution of similar products. The differentiation between intra-state and interstate activities to define a compounding manufacturer could create patient safety concerns by unintentionally creating a safe haven for entities and individuals engaging in intra-state activities who have the intent to simply avoid the different and Federal-based requirements for interstate activities.

We ask the committee to reconsider this provision and instead include the preparation of non-patient-specific, sterile prepared products for intra-state activities as a defining component of a compounding manufacturer and within the scope of authority of the FDA.

CONCLUSION

As stated earlier in our statement, the other provisions of the proposed legislation that address the safe preparation of medications and products for patients align well with the approaches suggested and recommended by the States. The legislation proposed by the committee demonstrates the hard work conducted to understand a complex area of pharmacy practice that is necessary to ensure that patients receive the appropriate medications but must also be regulated effectively. The legislation distinguishes between compounding and manufacturing, defines a new category of manufacturing that balances effective regulation with reality, and carefully constructs allowances and prohibitions on the scope and activities of a compounding manufacturer in order to meet patient needs with the necessary protections. NABP appreciates this opportunity for input and is available to discuss our comments and the proposed legislation in greater detail.

Thank you.

The CHAIRMAN. Thank you very much, Mr. Catizone.
Mr. Coukell, again, welcome and please proceed.

STATEMENT OF ALLAN COUKELL, DIRECTOR, MEDICAL PROGRAMS, THE PEW CHARITABLE TRUSTS, WASHINGTON, DC

Mr. COUKELL. Chairman Harkin, Ranking Member Alexander, and members of the committee, thank you for the opportunity to testify. My name is Allan Coukell. I'm a pharmacist and director of drug and medical device work at the Pew Charitable Trusts, an independent research and public policy organization. Pew has a long focus on drug quality issues. I am pleased to be able to support the bipartisan proposal before you today.

Pharmacists have always compounded medicines, but the activities you seek to address are far removed from the traditional preparation of an individualized medicine for a single patient. Some compounding pharmacies now produce large volumes of drugs and ship thousands of units of high-risk or sterile products to clinics and hospitals across the country.

The fungal meningitis outbreak caused by contaminated steroid injections highlights the risk to patients. But it's only one recent case. Included with my written testimony is a summary of 19 more pharmacy compounding errors from the past decade. It includes 22 additional deaths, as well as meningitis, bloodstream infections, and at least 38 patients blinded or suffering vision loss caused by a compounded drug.

And it notes toxicities caused by super-potent products. For example, three people died in 2007 after receiving intravenous injections for back pain that were eight times the labeled strength.

Recent FDA inspections raise further concerns. For example, a New Jersey compounder 2 months ago recalled all of its products because of potential mold and particulates in the vials. Another case this year involved a Georgia compounder that conducted a nationwide recall because of serious eye infections.

Congress has long grappled with these risks. Section 503(A) of the Food, Drug, and Cosmetic Act was passed in 1997 and later partially struck down by the courts. Members of this committee have tried again. In 2007, legislation was strongly opposed by the compounding industry and did not pass. Today, FDA's legal authority remains unclear.

The proposal before you offers the opportunity to finally address some high-risk compounding activities, and it has the following strengths: It addresses sterile products, which are especially high risk. It includes facilities that sell in multiple States and, therefore, captures many of the largest operations, though not all of them. And it contains safeguards that will help prevent compounders undermining gold standard FDA-approved drugs.

Under this legislation, a new category of compounding manufacturers would need to comply with applicable good manufacturing practices, as do pharmaceutical companies making FDA-approved drugs. This would be an improvement on the USP standards used in many States which were not designed for large-scale anticipatory production.

This point was stressed strongly by experts who spoke at a recent compounding summit hosted by Pew, ASHP, and the American Hospital Association. The current proposal recognizes that FDA is the appropriate agency to oversee this higher quality standard.

While the goal is to ensure the quality of compounded products, patients, doctors, and pharmacists should prefer FDA-approved drugs whenever possible. Only the latter go through premarket review to establish safety, efficacy, bioequivalence, along with the pre-approval of manufacturing methods and facilities. So it's important that this new regulatory scheme not encourage compounding at the expense of traditional manufacturing.

This draft contains a number of important safeguards. First, it clarifies that certain products may not be compounded by anyone, and that certain ingredients may not be used in compounding. It's also clear that the compounder may not make a copy or a variation of a marketed drug unless that drug is in shortage. We support the prohibition on wholesaling compounded drugs which will further reduce incentives to circumvent the FDA approval process.

Appropriately, these safeguards apply to all compounders and not just compounding manufacturers. Therefore, to support FDA's enforcement, we urge the committee to allow FDA to access records during inspections of all pharmacies, which will also allow the Agency to investigate whether a pharmacy is actually a compounding manufacturer.

Let me note that there are some important areas of risk not addressed by this proposal. First, companies that sell products within

a single State will continue to operate without FDA oversight. That means that identical products produced under identical conditions in identical volumes will be subject to different regulatory schemes. No State enforces GMP, and States vary widely in their ability to oversee large-scale compounding.

Second, this proposal does not address non-sterile compounding regardless of scale, even though improperly compounded tablets or capsules also have the potential to cause harm. Despite the areas not addressed, this bipartisan proposal is an important step toward addressing a longstanding risk to patients.

I thank you for your leadership and welcome any questions.

[The prepared statement of Mr. Coukell follows:]

PREPARED STATEMENT OF ALLAN COUKELL

Dear Chairman Harkin, Ranking Member Alexander and members of the committee, thank you for the opportunity to testify on your proposal to improve the safety of pharmaceutical compounding.

My name is Allan Coukell. I am a pharmacist and director of drug and medical device work at the Pew Charitable Trusts, an independent, nonpartisan research and public policy organization.

Pharmacists have always compounded medicines—it is the origin of the profession—but the activities you seek to address today are far removed from the traditional practice of preparing individualized medicines for one patient at a time.

Today, some compounders produce large volumes of drugs, often manufacturing them before a prescription is received, shipping many thousands of units—high-risk or sterile products—to clinics and hospitals across the country.

The regulatory framework has not kept up with this changing industry. Traditionally, States oversee pharmacy practice and the FDA oversees drug manufacturing. But compounding falls into a grey zone. In a very broad sense, FDA has the authority to regulate some compounding activities, but it is not at all clear how far that authority goes. Nor are there formalized mechanisms to divide the oversight of compounding between the States and FDA.

EXAMINING THE RISKS

The epidemic caused by the New England Compounding Center is but the most recent case highlighting the risks to patients.

That outbreak has been associated with 53 deaths so far and nearly 700 serious infections. Included with my testimony is a Pew summary that describes 19 additional pharmacy compounding errors since 2001.¹

The list includes 22 additional deaths, as well as serious infections—meningitis, bloodstream and at least 38 patients who suffered partial or complete loss of vision—but also patients harmed by sub-potent or super-potent doses. For example, in 2007 three people died after receiving intravenous colchicine that was *eight times* the labeled strength.²

Recent inspections of compounders raise further concern: Two months ago, the FDA announced a recall of all of the products manufactured by a New Jersey compounder because of potential mold contamination. The FDA press release referred to “visible particulate contaminants” in what was supposed to be a sterile product.³ Also this year, a Georgia compounder conducted a nationwide recall of sterile products after reports of serious eye infections.⁴

APPROPRIATE OVERSIGHT AND QUALITY STANDARDS

Congress has long grappled with these risks. The current section 503(A) of the Food, Drug and Cosmetic Act was passed in 1997. After the courts struck down parts of that provision, members of this committee tried again to create meaningful Federal oversight of certain compounding activities. But that legislation was strongly opposed by the compounding industry, and did not pass. Today, FDA’s legal authority remains unclear. Even as the Agency steps up its oversight of compounders, its ability to access records has been challenged.⁵

The proposal before you today offers an opportunity to finally address some, though not all, high-risk compounding activities. It has the following strengths:

- It addresses sterile products, which are particularly high risk;

- By including facilities that sell in multiple States, it will capture many of the largest operations; and
- It contains safeguards that will help prevent compounders from undermining “gold-standard,” FDA-approved drugs.

INCREASED FEDERAL OVERSIGHT

The legislation creates a new category of FDA-regulated “compounding manufacturers”—compounders that produce sterile products in anticipation of a prescription and who sell product outside the State in which it is created.

The bill would require compounding manufacturers to comply with the same manufacturing quality standards, known as good manufacturing practices (GMPs), that apply to pharmaceutical companies making FDA-approved drugs.

This recognizes that the U.S. Pharmacopeial standards (chapter 797) used in many States are unsuited to large-scale anticipatory production. Few recently joined with the American Hospital Association (AHA) and the American Society of Health-System Pharmacists (ASHP) to co-host a pharmacy compounding summit that heard from experts who stressed this point strongly. The FDA, and not State pharmacy boards, is the appropriate agency to enforce GMPs.

Using limited resources wisely necessitates addressing the largest potential public health problems first. That means, in part, ensuring quality standards at facilities that produce large numbers of doses. While not perfect, we believe that the proposed framework for interstate sales would capture a meaningful portion of the highest risk compounding.

However, we urge the committee to not exclude mixing and reconstituting of drugs in accordance with manufacturer label from the definition of compounding manufacturer. If these ostensibly sterile products are mixed in large volume under unsanitary conditions, it could represent a significant public health risk.

In addition, the definition of compounding manufacturer should include repackagers of preservative-free syringes and mini-bags or other units of sale and should not be limited to repackagers of preservative free vials.

COMPOUNDED PRODUCTS MUST NOT DISPLACE FDA-APPROVED DRUGS

It is important to note that while compounding manufacturers will be subject to FDA oversight of and quality standards, their products will not have gone through the pre-market approval process that brand and generic drug companies go through to demonstrate safety, efficacy and bioequivalence, along with pre-approval of manufacturing methods and facilities.

Because of those differences, compounded medicines can never be an adequate substitute for FDA-approved drugs. It is important this new regulatory scheme not encourage compounding at the expense of traditional manufacturing, and we believe the draft contains a number of important safeguards.

First, the bill clarifies that certain products may not be compounded by anyone, and that certain ingredients may not be used in compounding. It gives the FDA the authority to specify these products and ingredients, and restricts compounding from bulk to ingredients that are described by a USP monograph or are in an already-approved product.

The draft is also clear that a compounder may not make a copy or a variation of a marketed drug, except when that drug is in shortage. An exception allows variations compounded from bulk drugs to address specific medical needs, but only when a prescriber communicates in advance of the compounding that the drug would make a serious difference for the patient.

We also support the provisions that prohibit the wholesale of compounded drugs, which further reduces incentives to circumvent the FDA drug-approval process.

Appropriately, these important safeguards apply to all compounders, not just to compounding manufacturers. Therefore, to support FDA’s enforcement of these safeguards, we urge the committee to allow the FDA to access records during inspections of all pharmacies, not just compounding manufacturers. Further, the Agency must be able to investigate a company to determine whether it is, in fact, a self-identified “traditional compounder” or is actually a compounding manufacturer. A critical tool within such an investigation is access to records.

AREAS OF RISKS THAT ARE NOT ADDRESSED

It is important to understand which activities FDA would not regulate under this legislation, and the potential risks to patients.

First, large-scale sterile compounding operations that operate *within a single State* will continue to operate without FDA oversight. This means that identical products produced under identical conditions in identical volumes will be subject to

different regulatory schemes, depending on the accident of whether or not they are sold in one State or two. And, as our compounding summit heard, State pharmacy regulators vary widely in their ability to oversee large-scale compounding. Indeed, some States have elected not to register or provide oversight to such facilities. No State enforces quality standards equivalent to Good Manufacturing Practices.

Second, this proposal does not address *non-sterile* compounding, regardless of scale. Pew supports prioritized oversight of sterile products, but we note that there are a number of non-sterile compounded drugs, such as compounded “bioidentical” hormone replacement pills, that are widely distributed. Compounded oral dosage forms have the potential to cause harm by both impurities and sub- or super-potency.

JURISDICTIONAL ISSUES

Finally, we recommend that the committee consider allowing both Federal and State jurisdiction for entities that wish to engage in compounding manufacturing and pharmacy practice. We believe FDA’s oversight responsibility would still be clear, driven by the framework outlined in this bill. Entirely preventing a compounding manufacturer from engaging in any traditional pharmacy practice may be difficult, and where any entity engages in pharmacy practice, they must be licensed and overseen by appropriate State authorities.

CONCLUSION

The business of compounding has changed dramatically over the last 30 years and the regulatory framework has not kept pace. The lines of authority are unclear and there are significant gaps in oversight that leave much high risk, high volume pharmacy compounding almost unregulated. The lack of a meaningful regulatory framework may have guaranteed the kind of tragedy seen last fall, and that we will see again if Congress does not enact meaningful and enforceable rules to govern compounding. This bi-partisan draft legislation is an important step forward.

We thank you for your bipartisan leadership, and urge swift action to protect patients and avoid further senseless deaths.

Thank you for the opportunity to testify, and I welcome your questions.

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The Pew Charitable Trusts
Appendix B—U.S. Illnesses and Deaths Associated With Compounded Medications
(2001–Present) *

| Year | States | Reported cases | Reported deaths | Adverse events | Compounding error | Product |
|----------|-----------------------------------------------------------------------------|----------------|-----------------|------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| 2012 ... | FL, GA, ID, IL, IN, MD, MI, MN, NC, NH, NJ, NY, OH, PA, RI, SC, TN, TX, VA. | 733 | 53 | Fungal meningitis and other infections. | Contamination ¹ | Spinal injections: preservative-free sterile methylprednisolone acetate. |
| 2012 ... | CA and six other States. | 33 | | Fungal eye infection; 23 cases of partial to severe vision loss. | Contamination ² | Eye injections: Brilliant Blue-G (BBG) retinal dye and triamcinalone. |
| 2011 ... | FL, TN | 21 | | Bacterial eye infection; one case of meningitis and encephalitis; four cases of loss of eyesight; three patients had eye removals. | Contamination ³ | Eye injections: intravitreal bevacizumab (Avastin) injections. |
| 2011 ... | CA | 5 | | Blindness | Unintended presence of another medication ⁴ . | Eye injections: intravitreal bevacizumab (Avastin) injections. |
| 2011 ... | AL | 19 | 9 | Bacterial bloodstream infection. | Contamination ⁵ | Parenteral nutrition solution. |
| 2010 ... | IL | 1 | 1 | Fatal overdose | Dose of sodium 60 times stronger than ordered ⁶ . | IV solution: sodium chloride. |
| 2007 ... | WA, OR | 3 | 3 | Fatal overdose | Dose of colchicine eight times stronger than labeled concentration ⁷ . | IV solution: colchicine. |
| 2007 ... | MD, CA | 8 | | Bacterial bloodstream infection. | Contamination ⁸ | IV solution: fentanyl. |
| 2004–6 | MI, MO, NY, SD, TX, WY. | 80 | | Bacterial bloodstream infection. | Contamination ⁹ | IV flush syringes: heparinized saline. |
| 2006 ... | OH | 1 | 1 | Fatal overdose | Dose of sodium chloride stronger than ordered ¹⁰ . | Chemotherapy infusion. |
| 2006 ... | NV | 1 | 1 | Fatal overdose | Dose of zinc 1,000 times stronger than ordered ¹¹ . | Neonatal parenteral nutrition solution. |
| 2005 ... | | 2 | | Bacterial bloodstream infection. | Contamination ¹² .. | IV flush vials: preservative-free heparinized saline. |
| 2005 ... | MN and one other State. | 6 | | Bacterial eye infection; all cases had partial or complete loss of vision; two patients had eye removals. | Contamination ¹³ .. | Eye solution: trypan blue. |
| 2005 ... | VA | 5 | 3 | Systemic inflammatory response syndrome. | Contamination ¹⁴ .. | Heart infusion: cardioplegia. |
| 2005 ... | CA, NJ, NC, NY, MA. | 18 | | Bacterial bloodstream infection. | Contamination ¹⁵ .. | IV solution: magnesium sulfate. |
| 2004 ... | CT | 2 | | Bacterial bloodstream infection. | Contamination ¹⁶ .. | IV flush syringes: heparin-vancomycin. |
| 2004 ... | MO, NY, TX, MI, SD. | 64 | | Bacterial bloodstream infection. | Contamination ¹⁷ .. | IV flush syringes: heparinized saline. |
| 2002 ... | NC | 5 | 1 | Fungal meningitis and sacroiliitis. | Contamination ¹⁸ .. | Spinal injections: methylprednisolone acetate. |

The Pew Charitable Trusts—Continued
Appendix B—U.S. Illnesses and Deaths Associated With Compounded Medications
(2001–Present) *

| Year | States | Reported cases | Reported deaths | Adverse events | Compounding error | Product |
|----------|----------|----------------|-----------------|------------------------------------------------------------------------------------------------------------|--------------------------------|--------------------------------------------|
| 2001 ... | CA | 11 | 3 | Five cases of bacterial meningitis; five cases of epidural abscess; one patient had an infected hip joint. | Contamination ¹⁹ .. | Spinal or joint injections: betamethasone. |
| 2001 ... | | 4 | | Bacterial bloodstream infection. | Contamination ²⁰ .. | IV infusion: ranitidine. |
| Total | | 1,022 | 75 | | | |

* The Pew Charitable Trusts has identified 20 pharmacy compounding errors associated with 1022 adverse events, including 75 deaths, since 2001. Contamination of sterile products was the most common compounding error, though some incidents were the result of pharmacists' and technicians' miscalculations and mistakes in filling prescriptions.

Pew's drug safety project works to ensure a safe, reliable pharmaceutical manufacturing and distribution system. For more information, visit www.pewhealth.org/drugsafety.

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The CHAIRMAN. Thank you, Mr. Coukell.

And now we’ll turn to Mr. Miller. Welcome back. Please proceed.

STATEMENT OF DAVID G. MILLER, EXECUTIVE VICE PRESIDENT AND CEO, INTERNATIONAL ACADEMY OF COMPOUNDING PHARMACISTS, MISSOURI CITY, TX

Mr. MILLER. Thank you very much, Mr. Chairman. My name is David Miller, and on behalf of the International Academy of

Compounding Pharmacists, it is a pleasure to be back before the committee and also to have been actively involved with your committee and staff in the creation of this draft proposal.

I want to keep my comments today focused on three major points. One is consistency, one is accountability, and one is on patient protection. First and foremost, I want to commend the committee for preparing this draft in a manner that gained the input of the pharmacy and physician community, the veterinary community, and the Food and Drug Administration. I think we're close. We're not there yet, but we're close.

I want to speak first and foremost to the issue of consistency and clarity. In the current draft bill, we see that there are some significant discrepancies between proposed language and what we've already seen either at the State level or has been enacted at the State level in the first few months of 2013.

Since the tragedy in Massachusetts began back in October, there have been 53 individual State bills introduced and actively considered, and some have already been enacted. As Senator Mikulski said, in my home State of Maryland, we have already moved forward there. Twenty-seven State boards of pharmacy are actively overhauling all of their regulations. It's very important as we look at this draft language that we ensure that the definitions used in the Federal statute that will eventually be enacted are consistent with how pharmacy is regulated at the State level.

I'll give you a couple of quick instances. We have talked about the preparation of medications in advance of a prescription as being one of the potential tests, especially in the sterile medication environment, that would place someone into this non-traditional manufacturing category, this compounding manufacturing category.

It's important to understand that as compounding pharmacists, we do prepare medications before prescriptions are received in our practices. The reason we do that is that our national standards under the U.S. Pharmacopeia require us to prepare batches and test them so that we can be confident in their quality.

So we have to make sure that our definitions and our language are consistent from the Federal level and then down into the State level. We see that also with a lack of recognition of physician office use prescribing, which many States have available, and yet the current language that we have before us would essentially ignore the existence of that and raise questions about the consistency and clarity of the application of this language.

Finally, I also want to point out, under the category of clarity, that we have proposed in this legislation that veterinary drugs would be regulated in a markedly different way than we would humans. For example, on the human side, we would continue to have in some manner an expanded do-not-compound list. Yet on the veterinary side, we're creating something completely different and, again, inconsistent by having a—these are the ones you can compound.

So we believe, based especially upon our conversations and the testimony that you heard back in November, consistency in law at the Federal and State level must be addressed. We're close, but not quite there, and some of our recommendations, we hope, will be taken into consideration.

Accountability. I think one of the things that we discussed back in November was the simple fact that the pharmacists at the New England Compounding Center let their patients down, they let their system down, and they let their regulators down. We also now know, based on testimony back in November and then again most recently from Commissioner Hamburg before the House Energy and Commerce Committee, that our regulatory agencies also let us down.

We need to be, in this bill, ensuring that there is accountability and transparency of action. Specifically, we are very concerned as an organization about the do-not-compound list. The Food and Drug Administration has had such a list since 2003. That's the last time it's been updated. That's 10 years ago.

We now know that there are medications that have been withdrawn from the market from traditional manufacturers that represent serious public health and safety issues. They don't appear on the do-not-compound list. IACP has recommended in its comments to the committee that accountability—first and foremost, congressional oversight of the agency—must be included to assure that everyone's feet are being held to the fire.

Last, patient protection. Our objective as a professional organization, as pharmacists that take care of patients on a daily basis, is that this does not happen again. No patient, regardless of where they are, should expect to have any variation in the quality and safety of the medication they receive.

That is one of the reasons we are also strongly opposed to any exemption of any type of pharmacy practice. Hold us all accountable. Hold us all to the same consistent law. And with that, all of us together will be ensured that we can provide patients with the protection that they should receive.

Thank you, sir.

[The prepared statement of Mr. Miller follows:]

PREPARED STATEMENT OF DAVID G. MILLER

Good morning Chairman Harkin, Ranking Minority Member Alexander and Senate HELP Committee members. On behalf of the International Academy of Compounding Pharmacists (IACP), I am pleased to stand before your committee to offer the insights of the International Academy of Compounding Pharmacists (IACP) and our recommendations about the draft legislation put forward by the committee. Specifically, IACP wants to take this opportunity to comment on the compounding pharmacy legislation and how it will likely impact our industry, patients and practitioners.

IACP applauds the steps the committee and the U.S. Senate are taking to ensure that compounded medications are as safe as they can be. IACP believes that the safety of patients must always be the first consideration of any pharmacy-oriented public policy.

We have reviewed the draft and we see that there are some aspects that will need further discussion and refinement, and we intend to work with the committee on these. The draft does not contain any provisions that speak directly to USP standards, which are aimed at raising the quality of compounded medications. Additionally, IACP is concerned that some provisions may reduce patient and physician access to customized medications, the very services that compounding pharmacists provide.

IACP reiterates its position that State boards of pharmacy are responsible for the licensing and oversight of compounding pharmacies and the FDA is responsible for overseeing and regulating pharmaceutical manufacturers. We think the term "compounding manufacturer" and several of the definitions of that new category create more confusion and further blur the jurisdictional authority of regulators. IACP

will recommend improvements in the draft language to make the proposed categories more clear.

Most importantly, IACP is gravely concerned that compounding pharmacies located in hospitals and health systems have been exempted from many of the proposed changes. Such an exemption denies patients and their families the assurance, regardless of where they receive their medications, of the quality and safety that they deserve.

IACP appreciates the opportunity to work with the Senate HELP Committee to ensure that a tragedy like the one that occurred last year, when compounded preparations dispensed by a Massachusetts licensed pharmacy caused an outbreak of fungal meningitis, never happens again. It is with that crisis in mind that we have reviewed the draft legislation to determine if it will likely prevent a future scenario similar to that which occurred with NECC.

IACP is a non-profit professional association representing more than 2,700 pharmacists, technicians, students, and members of the compounding community who focus on the specialty practice of pharmacy compounding. The IACP is and has been committed to working in collaboration with State and Federal officials to ensure the safe practice of pharmacy compounding. Our ultimate goal is to ensure patient safety, while ensuring continued patient access to compounded medication necessary for their particular medical condition.

In December 2012, the Academy issued a series of recommended changes to State pharmacy laws and regulations that it believes will both enhance the protection of public health while preserving the professional decisionmaking of pharmacists in the selection and preparation of customized medication solutions.

These proposed changes address three key areas: inspection authority and adequate funding of all State Boards of Pharmacy; compliance with laws and regulations by all pharmacists and pharmacy technicians in all practice settings, as well as other health care practitioners involved in compounding; and adherence to nationally recognized quality standards. As you know, many States have already been working to enact or establish new laws and rules governing the practice of pharmacy compounding. IACP has been actively involved in those efforts in an attempt to strengthen and clarify appropriate and safe pharmacy practices. As a matter of fact, IACP has been actively engaged in these discussions—not to lessen oversight on pharmacy practices, but to encourage maximum patient safety protections, while ensuring that compounded medications do not become distinct as a result of what NECC—a rogue manufacturer—did.

IACP take strong issue with the terminology used throughout the bill to define the new category of manufacturer as a “compounding manufacturer.” Not only do we think this causes confusion, but it also seems to make the very practice of compounding synonymous with that of manufacturing. In fact, the practice of compounding is at the very root of pharmacy practice. Thus, IACP recommends that the new category be called “non-traditional manufacturing” and we have made those edits in the attached draft bill.

We ask the committee to keep in mind that a significant number of people have unique health needs that off-the-shelf, one-size-fits-all prescription medicines cannot meet. These include children, the elderly, and those for who manufactured drug products are not available in the appropriate strength, dosage form, or composition. For them, customized medications are the only way to better health and those valuable preparations are available only by compounding. Thus, there is a medical need for variations in medical dosages, delivery forms, the removal of excipients, etc. for various patient groups. That is why the very practice of compounding exists. IACP urges the committee to recognize this and not prohibit physicians from prescribing medications needed by both their human and animal patients.

Unfortunately, there are significant parts of the draft bill that have nothing to do with safety, but have to do with curtailing competition. IACP is aware that a good part of the anti-competitive language (not allowing dosage variations) comes from the large pharmaceutical manufacturers on both the human and animal side who wish to curtail compounding altogether. IACP hopes that the bill will remain focused on the end goal—that being patient safety, not getting rid of competition in the marketplace. It is not the time to attack compounding pharmacies from a commercial perspective as a result of other (monetary) motives. Safety should remain the objective of this bill.

IACP wants to make sure that any final bill moving through the Senate balanced in a manner that does not restrict a doctor's ability to prescribe and obtain compounded medications for those patients who require them as part of their necessary therapy. Moreover, manufacturers often discontinue a number of FDA-approved drugs that serve a limited population. In many of these cases, the only option left for doctors and their patients is to have a compounding pharmacist make the dis-

continued drug pharmaceutical grade ingredients obtained from an FDA-registered supplier.

IACP remains concerned about language in the bill that further brings practices under the domain of manufacturing.

(ii) that repackages a drug using sterile preservative-free single-dose vials or by pooling sterile drugs.

This is problematic for several reasons. Under this language, physicians who repackage in their offices would automatically become manufacturers. Additionally, this language was clearly added at the behest of a pharmacy manufacturer which has been trying to deter doctors from prescribing one of their drugs in lieu of another of their more expensive products. This language seems to have been added for competitive reasons, rather than safety reasons. This provision would also include a large number of home infusion pharmacies who fall under these criteria (the pooling provision) for administration of parenteral nutritional therapies. They would, under this provision, have to register and comply with the law as a manufacturer. IACP strongly recommends that this section be stricken.

While the IACP continues to strongly believe that the regulation of compounding should continue to be overseen by State Boards of Pharmacy and that improvements may need to be made to current State pharmacy laws (many States have already made changes, which IACP urges the Senate not to make moot), we understand the importance in determining what greater clarity in differentiating between drug compounding and drug manufacturing may be needed.

What we find interesting about this bill is the fact that you are taking away two existing regulatory authorities and streamlining it under one—the FDA (whose track record is not at all impressive—take Ameridose and their many problems as an example).

State Boards of Pharmacy, through their ongoing regular inspections, knowledge of unique State laws, regulations and rules, as well as having practicing pharmacists as their members who are engaged in day-to-day patient care, are in the best possible position to determine whether a pharmacy has exceeded its scope of practice or engaged in activities that may constitute manufacturing. That said, IACP recognizes that the oversight and regulation of prescription drug manufacturing rests with FDA, and that the Agency has the authority to identify and require the registration of any entities it believes are engaged in such activity.

IACP believes that language should be included in the legislation which requires a clear (and formal) exchange of information from the FDA to the State Boards and in the reverse—from the State Boards to the FDA if and when a pharmacy may be suspected of operating outside the parameters of pharmacy practice. Efficient and effective communication with State Boards of Pharmacy is essential to prevent the Agency's unilateral determination that a pharmacy's professional and business activities exceed the State specified scope of practice. Without such coordination any proposal is unlikely to achieve its goal or to improve public health safety.

The Academy also believes that some language contained in the bill micromanages the State Boards of Pharmacy on issues related to "office use" and "anticipatory compounding." Since many States have already taken action to address these issues, IACP does not believe it is appropriate for the Federal Government to regulate the practice of pharmacy. By specifically requiring only patient-specific prescriptions as part of the "test", the FDA appears to circumvent those individual State's laws, regulations and rules that enable prescribers to obtain compounded preparations for administration to or treatment of patients within their practices.

Office-use dispensing is the preparation, labeling, and dispensing of a medication by a pharmacist and pharmacy upon the receipt of a prescription or medical order from an identified authorized prescriber (e.g. physician, nurse practitioner, dentist, veterinarian, etc.) for that prescriber's use in the treatment of or administration to a patient during their normal course of medical practice. Office-use dispensing includes both manufactured prescription drug products and compounded preparations. Many States currently have provisions permitting office-use dispensing and other States are actively reviewing, clarifying, and issuing regulations on this very issue. Under the FDA concept, those appropriate State actions would essentially be nullified.

With regard to anticipatory compounding, the mere act of preparing a compounded medication prior to the receipt of a valid prescription or medical order issued by an authorized prescriber incorrectly places the focus on the preparation, rather than on the dispensing, shipment or distribution of a compounded medication. The true test should be whether or not a pharmacy has distributed a prescription medication in the absence of such a prescriber directive as defined within State

law. This is a much more appropriate test as it provides a potentially more accurate indicator of activities that may be deemed drug manufacturing.

IACP strongly opposes the draft bill's exclusion of health system pharmacies. We would note that health systems were the primary client of NECC and they purchased these injections in large quantities, without a patient script and without a doctor's order. In addition, they purchased these medications due to their low cost—not because of their quality. All legislation or regulation pertaining to compounding should cover all pharmacy practices, whether they are free-standing or located within a hospital or health care facility. There is no reason that patients within a hospital system should receive a substandard of care and safety. Indeed, many hospital patients assume they are more protected in health system environments when this has simply not been the case. ALL patient populations should be equally protected either within or without a hospital system. Exempting any practice site, such as hospitals, creates two distinctly different categories of patient safety protection. This is especially questionable in light of the volume and types of compounding done in hospital pharmacies, a substantial amount of which includes sterile compounded preparations.

Additionally, by creating a large loophole in a law designed to enhance safety for patients, the true goal of patient care is not achieved for all patients. Additionally, health systems are actively purchasing and acquiring other practices—they would, thus, fall into a different category and would no longer have to be compliant with this Act. The language also creates a potential concern for the Federal Trade Commission regarding restraint of trade and one could argue that this language allows for an uneven playing field and potential danger to patients in those health systems. Please see the attached documents discussing the rate of infection in health systems and the sheer volume of sterile compounding done in these institutions.

IACP urges the committee (if the goal is to truly enhance safety for *all* patients) to consider the implications of such an exemption on public safety and the perception of exempting any entity on the mere basis that it is located in a hospital or health care facility. While we understand that the application of any new rules and regulations may have to be modified to take into consideration other existing regulatory agencies and quality assurance agencies that oversee hospital safety and practices (i.e., the Joint Commission), such a challenge is manageable and should not outweigh the overall interest in ensuring patient safety.

With respect to an identifying label, IACP has formal guidelines for its members that requires all compounded preparations be labeled as such so that the prescriber and/or patient is readily aware that the medication has been compounded. IACP supports the labeling language included in the draft bill.

The IACP continues to point out that the recommendation to create and maintain a “do not compound” list by the FDA based upon patient safety already exists under FDCA section 503A(d)(1). Such a list was created by the Agency and is continually promoted to the compounding profession by the IACP to educate its members and others. The Academy respectfully points out to the committee that even given such authority under section 503A(d)(1), the Agency has not updated the current “do not compound” list in more than 10 years. The draft bill neglects to require a regular review and update of this list (allowing for public comment). IACP recommends that—given the fact the FDA has largely let this list lapse, that such language be included in the bill. In fact, several manufactured FDA-approved drug products have been withdrawn from the market for reasons of significant threat to patient safety; the Agency has never included those medications on the existing “do not compound” list. IACP believes that any changes to this list must be done in an open, structured and, most importantly, timely manner that solicits and accepts the position and opinions of the medical and pharmacy community. IACP also believes that if the collective professional community and the FDA determine that a product should not be compounded due to evidence of patient safety, it should also not be available from a manufacturer.

With regard to animal drug compounding, IACP strongly believes that the laws and regulations governing human compounding should be synonymous with those governing animal drug compounding. IACP believes that the bill should include language to statutorily permit compounding with bulk ingredients for both human and animals. The FDA should be allowed to continue to produce a list of permitted bulk drugs in food-producing animals only. IACP does not believe there should be a “positive list” developed by the FDA to allow certain specified ingredients from which animal compounds could be formulated. Rather, it should maintain the same “negative” list it does for the human side detailing those ingredients which have been removed from the market for safety or efficacy reasons and, thus, which should not be used in veterinary compounding. This would make human and veterinary compounding laws and regulations consistent and far less confusing.

IACP applauds the steps the committee and the U.S. Senate are taking to ensure that compounded medications are as safe as they can be. IACP believes that the safety of patients must always be the first consideration of any pharmacy-oriented public policy.

We have reviewed the draft and we see that there are some aspects that will need further discussion and refinement, and we intend to work with the committee on these. The draft does not contain any provisions that speak directly to USP standards, which are aimed at raising the quality of compounded medications. Additionally, IACP is concerned that some provisions may reduce patient and physician access to customized medications, the very services that compounding pharmacists provide.

IACP reiterates its position that State boards of pharmacy are responsible for the licensing and oversight of compounding pharmacies and the FDA is responsible for overseeing and regulating pharmaceutical manufacturers. We think the term "compounding manufacturer" and several of the definitions of that new category create more confusion and further blur the jurisdictional authority of regulators. IACP will recommend improvements in the draft language to make the proposed categories more clear.

Most importantly, IACP is gravely concerned that compounding pharmacies located in hospitals and health systems have been exempted from many of the proposed changes. Such an exemption denies patients and their families the assurance, regardless of where they receive their medications, of the quality and safety that they deserve.

In closing, IACP applauds the committee for addressing areas of Federal law that may need to be updated and clarified. Again, IACP would also urge you to not lose sight of the fact that pharmacy compounding is vital to our health care system and to ensuring patient access to appropriate medications for a variety of medical conditions. We appreciate the opportunity to provide our testimony to the committee on its draft bill and look forward to continuing our work with you on this important issue.

The CHAIRMAN. You meant in terms of intra-state as well as interstate?

Mr. MILLER. Intra-state.

The CHAIRMAN. Yes, I just wanted to make that clear.

Dr. Thompson, welcome back. Please proceed.

STATEMENT OF KASEY K. THOMPSON, PharmD, VICE PRESIDENT, OFFICE OF POLICY, PLANNING AND COMMUNICATIONS, AMERICAN SOCIETY OF HEALTH-SYSTEM PHARMACISTS, BETHESDA, MD

Mr. THOMPSON. Good morning, and thank you, Chairman Harkin, Ranking Member Alexander, and distinguished members of the committee, for holding this hearing. My name is Kasey Thompson, and I serve as vice president for Policy, Planning, and Communications with the American Society of Health-System Pharmacists. I'm here today to provide ASHP's perspective on the committee's draft proposal on pharmaceutical compounding.

As stated in previous testimony, in the interest of patient safety, ASHP supports closing the regulatory gaps for a category of commercial compounding outsourcers we are now referring to as compounding manufacturers. We applaud the committee's efforts to accomplish closing these gaps.

We believe this proposed legislation addresses the regulatory uncertainties that were caused through various challenges to Section 503(A) of the Food and Drug Administration Modernization Act of 1997. Importantly, the committee's proposal leaves traditional compounding as a core component of the practice of pharmacy under the purview of State boards of pharmacy.

ASHP strongly supports the creation of a category known as compounding manufacturer, which would fall completely within the

purview of the FDA. We further agree that not allowing a compounding manufacturer to register as a pharmacy in any State establishes a clear boundary between FDA jurisdiction and the jurisdiction of State boards of pharmacy. Being under the purview of the FDA gives the public the certainty of knowing exactly which regulatory body is accountable and will help prevent an entity like the New England Compounding Center from inappropriately operating as a pharmacy ever again and harming our patients.

The proposed legislation assures hospital and health system pharmacists, physicians, and other purchasers of compounded products that compounding manufacturers that prepare sterile products have taken the necessary steps to ensure their facilities meet the most rigorous current good manufacturing practices, have been inspected by the FDA, and, most importantly, do not pose a threat to the patients due to inadequate regulatory oversight.

ASHP agrees that commercially available products should not be compounded except to meet specific medical needs or if they are placed by the FDA on its drug shortage list. Furthermore, there should not be any loopholes in the law that would enable an entity to circumvent the drug approval process. We believe that the current drug approval process for new and generic drugs should be preserved as the gold standard and in no way minimized or circumvented.

ASHP supports the provision that exempts health systems from being designated as compounding manufacturers. We believe it is critical to make the distinction between health systems, which are fully accountable for the comprehensive care of the patient, and a compounding manufacturer that prepares and sells its products across State lines without a prescription or knowledge of the patient to a third party for administration.

In a hospital or health system, the same entity that compounds the medication is also responsible for the care of the patient. No medication compounded or otherwise prepared is administered to the patient unless there is a patient specific medication order.

Compounded medications prepared by pharmacy departments and all other medications used in hospitals and health systems are prescribed or ordered based on established relationships with the medical staff and other prescribers, all of whom are formally credentialed and privileged by the hospital or health system. Further, hospitals and health systems are not engaged in the retail sale of compounded products to other entities, but instead prepare and purchase compounded products for use on the patients being cared for in their hospital, health systems, and clinics.

Now, in the highly unlikely event that a hospital or health system ever did want to sell a sterile compounded product by engaging in interstate commerce to an outside entity that is not part of their system, then we believe the proposed legislation as it is currently written would require them to become listed as a compounding manufacturer, which we would support.

What makes this scenario highly unlikely is that a hospital or health system that becomes a compounding manufacturer would then not be allowed to be a pharmacy, which would prevent them from accomplishing their patient care mission. Hospitals are in the business of caring for patients, not manufacturing pharmaceuticals.

Hospitals also have pharmacy and therapeutics committees comprised of medical, administrative, and pharmacy staff that allow safe and effective products to be placed on their approved drug formularies. They also have well-established quality improvement, infection control, and risk management committees, as well as adverse event monitoring and reporting systems.

Another distinguishing factor for health systems is that they must comply with CMS Hospital Conditions of Participation and are accredited by quality improvement organizations such as the Joint Commission. These are just a few of the examples of how hospitals and health systems function differently from other care settings and are, therefore, appropriately excluded from the class of compounding manufacturer in the draft legislation.

In closing, I want to thank you, Chairman Harkin and Ranking Member Alexander, for the bipartisan leadership that you have demonstrated in the interest of protecting the public health and for holding this hearing and putting forth a thoughtful and well-developed proposal. ASHP believes this proposal provides the proper pathway forward to protect patients and to ensure that a harmful event like the meningitis outbreak of 2012 will never happen again. We are completely committed to working with you and the committee to see that this legislation gets passed into law.

Thank you.

[The prepared statement of Mr. Thompson follows:]

PREPARED STATEMENT OF KASEY K. THOMPSON, PHARM.D

SUMMARY

The American Society of Health-System Pharmacists (ASHP) supports the draft legislation put forth by the Senate Committee on Health, Education, Labor, and Pensions in the wake of the Meningitis Outbreak of 2012 caused by tainted sterile products prepared by the New England Compounding Center. We believe the draft addresses the regulatory uncertainty that currently exists between State boards of pharmacy and the Food and Drug Administration (FDA) over sterile preparation entities that engage in interstate commerce of their products and do so without a prescription. In addition, the committee's proposal leaves traditional compounding as a core component of the practice of pharmacy under the sole purview of the State boards of pharmacy.

ASHP strongly supports the creation of a category known as "compounding manufacturer," which would fall completely within the purview of FDA. We further agree that not allowing a compounding manufacturer to register as a pharmacy in any State establishes a clear boundary between FDA jurisdiction and the jurisdiction of State boards of pharmacy. The proposed legislation assures hospital and health-system pharmacists, physicians and other purchasers of compounded products that compounding manufacturers that prepare sterile products have taken the necessary steps to ensure their facilities meet rigorous standards and have been inspected by the FDA.

ASHP supports the provision that appropriately exempts health systems from being designated as a compounding manufacturer. Hospitals are fully accountable for the comprehensive care of their patients and do not introduce compounded products into interstate commerce. Further, we support the do not compound list, user fees, adverse event reporting, and the prohibition of compounding commercially available drugs except for those in shortage.

Good morning and thank you Chairman Harkin, Ranking Member Alexander, and distinguished members of the committee, for holding this hearing. My name is Kasey Thompson, and I serve as vice president of Policy, Planning and Communications at the American Society of Health-System Pharmacists (ASHP). I am here today to provide ASHP's perspective on the committee's draft proposal on pharmaceutical compounding.

As stated in previous testimony, in the interest of patient safety, ASHP supports closing the regulatory gaps for a category of commercial compounding outsourcers that we now refer to as “compounding manufacturers,” and we applaud the committee’s effort to accomplish closing these gaps.

We believe this proposed legislation addresses the regulatory uncertainties that were caused through the various challenges to Section 503A of the Food and Drug Administration Modernization Act of 1997. Importantly, the committee’s proposal leaves traditional compounding as a core component of the practice of pharmacy under the sole purview of State boards of pharmacy.

ASHP strongly supports the creation of a category known as “compounding manufacturer,” which would fall completely within the purview of FDA. We further agree that not allowing a compounding manufacturer to register as a pharmacy in any State establishes a clear boundary between FDA jurisdiction and the jurisdiction of State boards of pharmacy. Being under the purview of the FDA gives the public the certainty of knowing exactly which regulatory body is accountable, and will help prevent an entity like the New England Compounding Center from inappropriately operating as a pharmacy ever again.

Simply put, we believe the committee got it right with this proposed legislation. The proposed legislation assures hospital and health-system pharmacists, physicians, and other purchasers of compounded products that compounding manufacturers that prepare sterile products have taken the necessary steps to ensure their facilities meet the most rigorous Current Good Manufacturing Practices, have been inspected by the FDA, and most importantly, do not pose a threat to our patients due to inadequate regulatory oversight.

Under the proposal, health care providers will have the assurance that if they purchase an out-source sterile product from a compounding manufacturer, wherever it is located throughout the country, that the product they purchase has come from an FDA-inspected and FDA-approved facility. We also agree that a compounded drug sold to a health care entity by a compounding manufacturer should be labeled “not for resale.”

ASHP agrees that commercially available products should not be compounded except to meet specific medical needs or if they are placed by the FDA on its drug shortage list. Furthermore, there should not be any loopholes in the law that would enable an entity to circumvent the drug approval process. We believe that the current approval processes for new and generic drugs should be preserved as the gold standard, and in no way minimized or circumvented.

ASHP supports the provision that exempts health systems from being designated as compounding manufacturers. We believe it is critical to make the distinction between health systems—which are fully accountable for the comprehensive care of the patient—and a compounding manufacturer that prepares and sells its products across State lines without a prescription or knowledge of the patient to a third party for administration.

In a hospital or health system, the same entity that compounds the medication is also responsible for the care of the patient. No medication, compounded or otherwise prepared, is administered to the patient unless there is a patient-specific medication order. Compounded medications prepared by pharmacy departments and all other medications used in hospitals and health systems are prescribed or ordered based on established relationships with the medical staff and other prescribers, all of whom are formally credentialed and privileged by the hospital or health system. Further, hospitals and health systems are not engaged in the retail sale of compounded products to other entities, but instead prepare and purchase compounded preparations for use on the patients being cared for in their hospital, health system, and clinics.

Hospitals also have Pharmacy and Therapeutics Committees comprised of medical, administrative, and pharmacy staff that only allow safe and effective products to be placed on their approved drug formularies. They also have well-established quality improvement, infection control, and risk management committees as well as adverse event monitoring and reporting systems. Another distinguishing factor for health systems is that they must comply with CMS Hospital Conditions of Participation, and are accredited by quality improvement organizations such as The Joint Commission and DNV Healthcare, both of whom have deemed status with Medicare. These are just a few examples of how health systems function differently than other care settings and are therefore appropriately excluded from the class of compounding manufacturers in the draft legislation.

We support the definition of “health system” in the provision in the bill that defines traditional compounder. However, it may need to be revised to reflect contemporary health systems that include ambulatory clinics and infusion centers under their common control. We have submitted comments to the committee that raise

this point and look forward to working with other hospital organizations and committee staff to resolve this need for language that reflects the various components of today's health systems.

ASHP supports the provisions in the draft legislation that grant FDA the authority to designate a list of drugs that should not be compounded. There are complex medications with mechanisms of action or delivery systems that should not ever be compounded. In addition, we agree that the FDA should identify bulk substances that should not be used in compounding.

We agree with the draft language requiring compounding manufacturers to report adverse drug events to the FDA MedWatch program and to have a licensed pharmacist directly supervising the compounding operations.

Finally, we support the establishment of user fees for compounding manufacturers in order to provide the FDA with adequate resources to regulate their activities. We also ask that Congress continue to consider increasing FDA's budget appropriation so that it can fulfill its vast global public health mission.

In closing, I want to again thank you Chairman Harkin and Ranking Member Alexander for the bipartisan leadership you have demonstrated in the interest of protecting the public health, and for holding this hearing and putting forth a thoughtful and well-developed legislative proposal. ASHP believes this proposal provides the proper pathway forward to protect patients and ensure that a harmful event like the meningitis outbreak of 2012 will never happen again. We are completely committed to working with you to help get this important legislation passed into law.

Thank you.

The CHAIRMAN. Thank you very much, Dr. Thompson.

We'll now start a round of 5-minute questions. I'll start with Mr. Catizone and go right down.

Does this legislation create a clear line regarding which entities FDA would regulate?

Mr. CATIZONE. Yes, sir.

The CHAIRMAN. Mr. Coukell.

Mr. COUKELL. Yes.

The CHAIRMAN. Mr. Miller.

Mr. MILLER. Yes, with some definitions.

The CHAIRMAN. Dr. Thompson.

Dr. THOMPSON. Yes.

The CHAIRMAN. Does the draft provide FDA the tools it needs in terms of both authorities and resources to oversee the pharmaceutical compounding?

Mr. CATIZONE. Yes, sir.

Mr. COUKELL. It provides some of the tools and a mechanism for resources. As I mentioned in my testimony, we think that the FDA may need greater access to records to be able to oversee the facilities it is charged with.

The CHAIRMAN. Mr. Miller.

Mr. MILLER. We believe so.

The CHAIRMAN. And Dr. Thompson.

Dr. THOMPSON. We think it provides the adequate resources through user fees. However, we continue to have concerns about the general funding to the FDA through appropriations to fulfill its public health mission, in general.

The CHAIRMAN. We all have that concern.

Mr. Catizone, let me ask you this now. When a State identifies a problem with a compounding pharmacy that is regulated by another State, what's the best way for that problem to be communicated to the regulating State? Does FDA have a role? Should the States talk directly to each other? Is this where the National Asso-

ciation of Boards of Pharmacy could be helpful? Help me to think this thing through.

Mr. CATIZONE. Yes, sir. Prior to the NECC situation, that communication channel was not effective. What we've now done is built the communication channels between the States through NABP, so when that happens, it's immediately reported to us, and we report it to all the other States. We will continue to implement and operate that system.

The CHAIRMAN. There is one lingering thing here, and maybe between Mr. Miller and Dr. Thompson—I can't remember exactly who. But Mr. Miller has testified that health systems should not be exempt—that we should put them all together—from being compounding manufacturers. Dr. Thompson testified in support of the exemption.

Mr. Catizone, where do you weigh in on this?

Mr. CATIZONE. We support the exemption because of the safety nets and oversight processes that exist within that shared one-ownership system among the hospitals.

The CHAIRMAN. Mr. Coukell, do you have a view on this?

Mr. COUKELL. If the question is whether a hospital pharmacy should be a pharmacy or a compounding manufacturer, clearly, they should be a pharmacy. As Dr. Thompson has mentioned, there are a number of additional mechanisms within a health system that ensure quality.

The CHAIRMAN. I'm not sure I understand that. If they are compounding, if a hospital is compounding, and they're not shipping it interstate or anything like that, but it's within their system, should they be exempted from being a compounding manufacturer?

Mr. COUKELL. Yes. We support the exemption.

The CHAIRMAN. I see.

Mr. Miller, you don't? Or what?

Mr. MILLER. If we go upon the definitions that have been created in the draft legislation to define a compounding manufacturer—the preparation of a sterile medication, the dissemination of that product intra-state, and without a previously issued prescription—then it doesn't matter whether that's a community-based pharmacy or a pharmacy that's affiliated with a health system. It should be consistently applied across the board. That is how you've defined a manufacturer as opposed to a traditional compounding pharmacy, be it local, be it in a hospital. I think we need to keep consistent.

The CHAIRMAN. Dr. Thompson.

Dr. THOMPSON. We clearly support the exemption. And, as I noted, I don't think hospitals are completely exempt here. If a hospital were to engage in preparing a product for commercial sale, and they sold that outside of their system, clearly, they should be required to be registered as a compounding manufacturer.

The CHAIRMAN. We understand that. But I think Mr. Miller is talking about a hospital that compounds for its own internal use.

Dr. THOMPSON. Yes. I don't agree with that, obviously. I mean, I think a hospital that—

The CHAIRMAN. Why shouldn't they? Give me some help here. Why not?

Dr. THOMPSON. As I just stated in my testimony, a hospital is fully accountable for the care of that patient. This is an apples to

oranges comparison. A hospital is not a manufacturer. A hospital is a patient care entity that's preparing a product and doing procedures for the patients they serve. They're not preparing large amounts of product and storing it in a warehouse for long periods of time. They're preparing that product in clean room conditions, taking it to the floor, administering it to that patient by licensed healthcare professionals that are accountable for that patient.

The CHAIRMAN. Do you have anything to add to that, Mr. Miller?

Mr. MILLER. Fundamentally, Mr. Chairman—and I thank you for pushing this issue. We have an image of a hospital as being the red brick building in our local community, and that's where hospital pharmacists practice, and we take care of patients within the facility. Today's modern health system is markedly different. For example, Johns Hopkins University now has hospitals throughout the State of Maryland, clinics, and home infusion and long-term care subsidiaries that operate throughout the mid-Atlantic region.

If we are to stop what happened at NECC where a business shipped medications interstate without prescriptions and not following the State law, whether that was a hospital pharmacy transferring it from the Baltimore campus to a clinic in Richmond, VA, we believe that that action is the same as you have defined for a compounding manufacturer.

My colleague at ASHP referenced retail or commercial sale. It shouldn't matter whether it's a sale associated with dollars. It is the movement and accountability of who is responsible ultimately for that medication. So, no, we would oppose the exemption.

Mr. CATIZONE. Mr. Chairman, may I add, please?

The CHAIRMAN. Mr. Catizone, my time has run out, but—fine. Go ahead.

Mr. CATIZONE. Two quick points as to why we think it should be exempted. No. 1, there is a patient prescription. It's within that closed system. It exists. Every aspect of that prescription is reviewed by the hospital. Drug interactions and contraindications are reviewed prior to that being dispensed.

No. 2, there are systems within that hospital system to make sure the product is properly prepared. And if there's a problem, there are infectious disease committees and other mechanisms to contain that within that system, react to that, identify the cause, and act appropriately.

The CHAIRMAN. Thank you. My time has run out.

Senator Alexander.

Senator ALEXANDER. Mr. Catizone, just so I understand our own draft here, if I'm a local drugstore in Tennessee, and I'm compounding a drug, and it's a sterile drug, and I have a specific prescription, and it's not on the do-not-compound list, I can still do that. Is that correct?

Mr. CATIZONE. Yes, sir.

Senator ALEXANDER. Is that right, Mr. Miller?

Mr. MILLER. Yes, sir.

Senator ALEXANDER. So we're not interfering with that with the draft bill.

Mr. Catizone, you say that you think the FDA also ought to take over the shipment within a State, intra-state shipment, of sterile compounded drugs without a prescription.

Mr. CATIZONE. Yes, sir.

Senator ALEXANDER. Do you want to amplify that?

Mr. CATIZONE. Yes, sir. As I said, we've been in over 150 pharmacies, and we've seen intra-state pharmacies as well as interstate pharmacies, and the risks are the same—large quantities, not following standards. And so if we just exempt the intra-state, we're going to put people at risk in that State to the same problems that we encountered before this incident.

Senator ALEXANDER. Mr. Miller, do you have an opinion?

Mr. MILLER. Senator Alexander, I'm sorry, but I feel like I'm on your flagpole, because that was a point you made before today and back in November. Intra-state shipment, intra-state compounding, is regulated by the State board of pharmacy.

Senator ALEXANDER. Within a State.

Mr. MILLER. Within, intra. That's right. And that's how the staff has worked, and this draft legislation appears to adequately define a traditional compounder. I disagree with my colleague at NABP. If it's intra-state, it belongs to the State.

At the same time, the minute it goes over the State line, then we have someone else on the flagpole, and that becomes the Food and Drug Administration. And that's, again, why we disagree with the concept of exempting a hospital. You move it out of the State, over the State line, that's when it becomes somebody else's regulatory authority.

Senator ALEXANDER. Mr. Catizone, you thought the FDA should—basically, there are some things in the draft that the FDA still could do with local drugstores that you thought ought to be out of the draft. Right?

Mr. CATIZONE. Yes, sir.

Senator ALEXANDER. Say that again. And I gather your point was that—that was the clarity point, to keep them—either they're going to be there, or they're not going to be there. Was that it?

Mr. CATIZONE. Yes, sir.

Senator ALEXANDER. Say that again.

Mr. CATIZONE. Yes, sir. By allowing the FDA access to records and giving them some authority over the State regulated activities, that's going to cause confusion. And let me use Dr. Miller's example that he used with the hospital exemption. If they're engaged in manufacturing, whether it's a hospital or a community pharmacy, he said that they should be regulated the same.

We're making the same contention with the exemption for intra-state. If they're manufacturing, they're not compounding. If there's not a prescription, and if it's sterile, it's not compounding. If they're compounding intra or inter, that should be State authority. But if they're manufacturing, inter or intra, that's the FDA.

Senator ALEXANDER. But on the first point, you say that if the FDA is given the authority to come in and inspect records of a local pharmacy that it doesn't otherwise regulate, that that adds confusion.

What do the rest of you think about that point?

Mr. COUKELL. I think if the Agency goes into a pharmacy as it does now, and it sees a product sitting in a sterile hood, they can't tell by looking at that product whether there's a prescription,

whether it's being sold across State lines. So it's hard to carry out the responsibilities here without the ability to access those records.

Senator ALEXANDER. Mr. Miller, Dr. Thompson.

Mr. MILLER. Two thoughts, Senator. First, section 704(A) has been in the statute since 1962, and the Agency has always had the ability through a regulatory administrative practice to obtain a court order or a subpoena or an administrative warrant to access those records. In the current environment, the State boards of pharmacy, who already have access to those records, are in co-operation with the FDA. We don't believe additional changes to a statute that has actually worked for a very long time are really mandated.

Senator ALEXANDER. Dr. Thompson.

Dr. THOMPSON. I think records, for the sake of inspecting records, should stay within the State. I think if the FDA has cause, if there's an identified risk, a contamination or something like that, that they shouldn't be prohibited from inspecting records.

Mr. CATIZONE. Senator Alexander, could I just add one point, please?

Senator ALEXANDER. Yes.

Mr. CATIZONE. The FDA has justification for making this request. So I would ask a consideration of the committee and then make a commitment to the committee. The States have not followed through in making that distinction between compounding and manufacturing in all the cases. And the FDA has been faced with dealing with that situation, and that's why they're requesting access. We see that situation, and we know we have to work with the States to repair that.

The consideration is the legislation as written is excellent. If we can move forward, and we can work with the States to repair that situation, then we would like a try to do that. If we can't, the commitment we're making is that we would come back to this committee and say, "The States have failed. They're not doing what they're supposed to be doing in this regard. Please turn this over to the FDA."

Senator ALEXANDER. Mr. Chairman, I want to ask just one question of Mr. Miller.

Mr. Miller, do you support this new category of compounding manufacturing? Do you just object to the name, or do you object to the new category?

Mr. MILLER. No, sir. We kind of object to the name, which is why we refer to them as a non-traditional manufacturer.

Senator ALEXANDER. But you don't object to the new category as a way to create accountability.

Mr. MILLER. With some minor modifications to the definitions. The conceptual—absolutely. In fact, in our original testimony and as we have consistently stated, the FDA has authority over drug manufacturing in the United States, period. There's no question about that. We need to refine that flagpole, or that bright, clear line that says when does a compounding pharmacy exceed its scope of practice, as was the case in Massachusetts.

The board of pharmacy makes that determination and says, "You're a manufacturer. You're no longer being a pharmacist." And that is the privilege of the board to tell me when my license has

been exceeded, and then turn me over to the FDA as a manufacturer.

The CHAIRMAN. Senator Warren.

Senator WARREN. Thank you, Mr. Chairman. I just want to examine some more of the role that State boards should play in overseeing the traditional compounding pharmacies. Obviously, this law anticipates that for intra-state work, this is going to be done entirely at the State level, and the same for interstate shipment of non-sterile products.

So following the outbreak at NECC in Massachusetts and the terrible events that resulted from that, my colleague, Congressman Ed Markey, from Massachusetts and his colleagues in the house launched an investigation just to determine what State pharmacies are doing in terms of overseeing these compounding labs.

I just want to read you some of the findings from the Markey report.

“No State boards of pharmacy require the pharmacies to disclose the amount of drug they are compounding or whether they’re sold across State lines. Thirty-seven State boards don’t track which pharmacies are performing sterile compounding. On average, States employ five inspectors with responsibility for inspecting all pharmacies, including the compounding pharmacies.”

That’s five.

In Massachusetts, that’s 1,179 pharmacies. In larger States, the number can be upwards of 2,000 pharmacies, with five inspectors, on average. And here’s the one that really got me. “Less than a quarter of the State boards provide inspectors any training to detect problems with sterile compounding.”

So, given that that’s the current state, my question is: What permanent changes do the States need to make in order to coordinate with the Federal law so that we really have some assurance that we have a comprehensive system that keeps all of our patients safe?

You’re nodding your head, Mr. Miller. So I’ll start with you.

Mr. MILLER. Thank you, Senator Warren. And I have to tell you the Commonwealth of Massachusetts actually had in place some of the best and most restrictive compounding pharmacy laws in the entire country. It is, indeed, a tragedy that this pharmacy intentionally concealed some of its actions from both State and Federal inspectors, and then even more so continued to operate in violation of those laws. How do we fix this?

Senator WARREN. But I have to interrupt you there, Mr. Miller, just to point out that we’ve done subsequent inspections and found that there continue to be—even after this tragedy, even after all the heightened awareness, there continue to be substantial violations of the basic rules of keeping these products clean and safe for consumers. So this is not a one off that we have a problem with.

Mr. MILLER. No, I agree. Within the Commonwealth itself, and also in some of the other States, as Congressman Markey’s report showed, we did not have regular inspections of compounding pharmacies. What we are seeing now in Massachusetts and in other States—where the boards are taking this seriously, hiring the necessary individuals with the proper training to conduct those inspec-

tions—is that we are uncovering things that should have been uncovered long ago.

So IACP, as a professional organization, immediately, in the fall, began putting out positions that our States need to take, fully fund, and hold our boards of pharmacy accountable for performing their responsibility, which is protecting the patients within the State.

Senator WARREN. And how many States are now in compliance with your suggestions?

Mr. MILLER. I don't know how many we have right now, Senator, because, as I mentioned before, we literally have bills rolling through various State legislatures. Maryland just passed theirs 2 weeks ago. Maine just introduced theirs 2 weeks ago. So it's something that is definitely in process.

Senator WARREN. Do you know that it's in process in all 50 States?

Mr. MILLER. Yes. That I can tell you. It is.

Senator WARREN. So we know it's in process. Here's what I want to know. What assurance do we have that what happens will be adequate, that it will happen in every State, and that there will continue to be enforcement after the lights have dimmed and the tragedy has faded from the memory of many people?

Mr. MILLER. Senator, I think that's a challenging question from the standpoint that those of us who are involved in this today will not forget it. Our boards of pharmacy, the individual pharmacists, the professional and public members that serve on those boards are committed to ensure that the systems are put into place—and I know Dr. Catizone can talk about that a little bit better than I can—that we set up a system that does not allow this to continue.

I do believe, however, you're right in asking the question: How do we know 10 years from now that we don't slack off?

Senator WARREN. We're not even to the point of slacking off. We haven't gotten there to be able to think about slacking off yet. And I want to ask if there is anything in the Federal law that says we will depend only on the States that have passed adequate laws to make sure that there is full safety for our patients. In other words, if the States fail to act, if there are loopholes, if only some of the States act, we're still going to be relying on those States. Is that right, under the statute that—

Mr. MILLER. With the regulation of the practice of pharmacy and the issuance of licenses for pharmacies and pharmacists, yes, you will continue to be reliant upon the States.

Senator WARREN. So we are only assuring patient safety in cases in which the State acts as well as the Federal Government acting. Is that right?

Mr. CATIZONE. No.

Senator WARREN. I'm getting yeses and nos. I'm sorry. I'm over my time, Mr. Chairman, but perhaps this is something we should—is that all right?

Go ahead, Mr. Catizone.

Mr. CATIZONE. Sure. The answer is no, and I think this is a very complex issue, but it can be broken down into very basic concepts. And I think Congressman Markey's report emphasize that and your questions do as well. If it's manufacturing, it's going to re-

quire GMPs and the FDA, whether it's intra-state or interstate. That mechanism is being built.

Senator WARREN. I understand.

Mr. CATIZONE. If it's traditional compounding, it's going to involve USP standards and the current State practice acts and regulations, which were not the problems with the NECC situation. It was the manufacturing of those products outside of that regulation. So the States are building the systems. They can regulate that. We're building the resources around them with it. If the FDA can do intra and interstate, you will have a permanent mechanism and the States will deal with it day to day.

Senator WARREN. I think we have a different response here.

Mr. COUKELL. Senator, the proposal will bring some facilities under FDA oversight using three tests, one of which is interstate sale. So facilities that sell within a single State that operate at the same scale would continue under State jurisdiction. One of the things that we heard strongly at the pharmacy compounding summit that we co-hosted with ASHP and the NABP participated in is that States vary widely in their ability to oversee this large-scale production. No doubt, there's activity going on, but it's very variable.

Senator WARREN. So you're telling me that we really have some serious gaps there, potentially.

Mr. COUKELL. Potentially.

Senator WARREN. Thank you very much.

Sorry, Mr. Chairman.

The CHAIRMAN. That's all right. Thank you, Senator Warren.

Senator Roberts.

Senator ROBERTS. Thank you, Mr. Chairman.

Thanks to all the panel members. I know you're busy, and to come here—this has been very helpful, I think, as we get into all the ramifications of the draft bill. We really tried very hard to ensure that we don't make laws after this 10-year effort without knowing the impacts, such as restricting patient access to life-saving medications.

I know that the regulatory process in Washington is such that it's probably the No. 1 issue in my State in regards to overkill—sub-regulatory guidance, people not even knowing about it, final rules that happen within 30 days, Executive orders, so on and so forth. The President even has an Executive order that says we desperately need for all the agencies—that you put up a yardstick in regards to cost and benefit, and I appreciate all of you trying to help us in that respect.

Mr. Miller, thank you especially. I thought there in 2007 that we'd end up on Front Street with guns drawn, but you put yours in the holster, and I have all your comments right here. And I have your—you mentioned definitions. They're in italics so they stand out, and this committee will go over your definitions. I'm glad to have you on the stagecoach. I don't know who's driving. Hopefully, we're driving the stage, and you can ride shotgun and make sure everything is OK. So we're going to do that.

I was going to ask you all if you're satisfied with the level of stakeholder input that has been allowed throughout the drafting process. All of your answers are yes. That saves a lot of time.

I'm caught up with the comments by Senator Warren and Senator Enzi. The local pharmacist does not need Federal inspectors going around the State. Let me point out that the FDA has already inspected about 30 pharmacies based on solid evidence of misconduct. You can work with the State board and gain access to records. You can work, as Mr. Miller has pointed out, by simply going through the warrant process.

You can get a warrant, you can work with the State board, and I think you could probably go into any pharmacy that has a very bad record, a lot of complaints, a lot of problems—hopefully not a medical disaster like we had with meningitis. And since FDA is already going into about 30 pharmacies—and I think they were prompted by that when I asked them why they're not—you can do this.

Now, Mr. Miller, there is a situation with Children's Mercy Hospital. They're located in Missouri, and they're a very well-known hospital and do amazing work. Four blocks away in Kansas, there is an annex to that. Guess what, by your definition, is going to happen? They're under the Missouri State Pharmacy Board, but under your suggestion, they would be put in this one category. I can't imagine you'd want to do that.

Mr. MILLER. The pharmacy on the Missouri side has a license issued by the State of Missouri.

Senator ROBERTS. That's correct.

Mr. MILLER. The pharmacy or the hospital on the Kansas side has a license issued by the State of Kansas.

Senator ROBERTS. Right.

Mr. MILLER. For all intents and purposes, that is, going back and forth, interstate. So would we expect that the preparation of a medication on the Missouri side transferred over across State—and, believe me, I'm from this area, so we go back and forth amongst States all the time. If it is for an individual patient and labeled as such—and that's what we've included as one of our recommendations in the exemption language—then we're fine.

If, however, the pharmacy on the Missouri side is preparing bulk—lots of sterile drugs to send down the street without any patient prescriptions prior to—that, essentially, is a duplicate of the definition of what we have for all other compounders.

Senator ROBERTS. All right. You made that clear. Let me just add that it was Quantrill who came in from Missouri to Kansas. We would never do that in Kansas, going the other way.

[Laughter.]

Mr. MILLER. As long as I'm not invited to Dodge City, I'm happy.

Senator ROBERTS. OK.

Thank you all for coming. I think my time is up, and I've used enough time, Mr. Chairman. Thank you so much.

Thank you all for your input.

Mr. MILLER. Thank you, sir.

The CHAIRMAN. Thank you all very, very much. This has been very informative, and I think I can safely say that no one has to be taken to Dodge City after this hearing. But I just want to thank you all very much.

Just in hearing the testimonies and the Q&As back and forth, I think we're pretty close. I think we're pretty close. We'll look at

some of the definitional things that you've suggested. When I hear that, I always think what's in a name, but sometimes, there's more than I think in a name. I don't know.

But I think we're pretty close. Our staffs will work together again as we have in an open system and resolve what little matters need to be resolved. But I think from the general tone of what I hear, I think we're very, very close to knowing what we need to do. Hopefully, again, working with Senator Alexander and others, we can have a markup sometime soon and move this legislation.

With that, the record will remain open for 10 days to allow members to submit questions and statements for the record. Thank you again very, very much for everything, and the committee will be adjourned.

ADDITIONAL MATERIAL

RESPONSE TO QUESTIONS OF SENATOR ENZI BY JANET WOODCOCK, M.D., CARMEN S. CATIZONE, M.S., RPH, DPH, ALLAN COUKELL, AND KASEY K. THOMPSON, PHARM.D.

DEPARTMENT OF HEALTH & HUMAN SERVICES,
FOOD AND DRUG ADMINISTRATION,
SILVER SPRING, MD 20993,
November 26, 2013.

Hon. TOM HARKIN, *Chairman,*
Committee on Health, Education, Labor, and Pensions,
U.S. Senate,
Washington, DC 20510-6300.

DEAR MR. CHAIRMAN: Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at the May 9, 2013, hearing before the Committee on Health, Education, Labor, and Pensions entitled "Pharmaceutical Compounding: Proposed Legislative Solution." This letter provides a response for the record to a question posed by Senator Mike Enzi, which we received on May 28, 2013.

If you have further questions, please let us know.

Sincerely,

SALLY HOWARD,
Deputy Commissioner,
Policy, Planning, and Legislation.

SALLY HOWARD FOR JANET WOODCOCK, M.D.

Question. FDA's comments on the discussion draft state that the Agency "must have access to records at traditional compounders" to enable the Agency to investigate traditional pharmacies who compound for potential violations of the new law. However, FDA has stated previously that traditional pharmacy must be preserved and FDA has previously never had access to pharmacy records to conduct enforcement actions. Can you please explain to me why FDA now believes that access to the records of traditional pharmacists is so necessary?

Answer. It is critical that FDA have clear authority to inspect pharmacies to determine the scope and nature of their operations to determine whether they are operating as compounding pharmacies or conventional drug manufacturers—generally subject to more stringent Federal requirements. In addition, FDA must be able to inspect pharmacies and review records to determine the source of a complaint or outbreak associated with a compounded drug that may be adulterated or misbranded under the Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA's ability to inspect in a timely manner any firm producing drugs is critical for effective oversight and regulation.

FDA should have clear ability to examine records such as records of prescriptions received, products shipped, volume of operations, and operational records such as batch records, product quality test results, and stability testing results. Such inspections are necessary to determine when a pharmacy exceeds the bounds of traditional compounding, to respond to public health threats, and to enforce Federal standards.

Under FDA's current inspection authority in section 704 of the FD&C Act, FDA's authority to inspect records at a pharmacy depends upon knowing certain facts about the pharmacy's operations that oftentimes can only be determined through inspection of records. The first of three criteria for being exempt from having records inspected is whether the pharmacy is operating in conformity with State law, a determination most readily made by a State and, in any case, likely dependent upon examining certain records. The second criterion concerns whether the pharmacy is dispensing prescription drugs without a prescription, but FDA must be able to inspect records to determine that fact. Similarly, the third criterion is whether the pharmacy is compounding drugs for sale other than in the regular course of its retail business, which is also something that would be difficult to determine without a full inspection of the facility, including an inspection of appropriate records. For each of these three criteria, FDA needs to examine records to determine whether the firm meets those criteria.

NATIONAL ASSOCIATION OF BOARDS OF PHARMACY,
MOUNT PROSPECT, IL 60056,
March 13, 2014.

COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS,
U.S. Senate,
Washington, DC 20510.

Your request for further information has been forwarded to my attention. Please feel free to let me know if you need additional information.

Best wishes,

MELISSA MADIGAN, PHARM.D, JD,
Policy and Communications Director.

MELISSA MADIGAN, PHARM.D, JD FOR CARMEN S. CATIZONE, M.S., RPH, DPH

Question. We intended, with this discussion draft, to preserve traditional pharmacy practice and compounding. However, we have received a number of comments indicating concern with the scope of compounding “in limited quantities” by traditional compounders. Can you please explain what you foresee as potential problems, if any, with this definition? How can the committee improve this language if it is a problem?

Answer. At the time of the hearing, NABP was highly concerned with pharmacies compounding drug products, especially sterile drug products, in large quantities “for office use” for administration to patients in prescribers’ office or clinics. As we all know, many States allowed this practice “in limited quantities,” but compounding pharmacies were either inadvertently or intentionally ignoring the “limited quantity” rule and compounding in extraordinarily large quantities. It was the type of practice that led to the widespread distribution of contaminated or unsafe compounded products, culminating with the NECC tragedy, which killed over 60 patients and injured nearly 700. Not long after the hearing, the Pharmaceutical Compounding Quality and Accountability Act was introduced, which addressed the concern by creating a new category of compounder called “compounding manufacturer” and prohibiting “for office use” compounding by pharmacies that are not “compounding manufacturers.”

ALLAN COUKELL

Question. We intended, with this discussion draft, to preserve traditional pharmacy practice and compounding. However, we have received a number of comments indicating concern with the scope of compounding “in limited quantities” by traditional compounders. Can you please explain what you foresee as potential problems, if any, with this definition? How can the committee improve this language if it is a problem?

Answer. The threshold for allowable anticipatory compounding by traditional compounders (TCs) is a longstanding area of confusion. The terminology used in section 503(A), as well as this bill, permits anticipatory compounding in “limited quantities” based on prescribing history. FDA’s compliance guide allows “very limited quantities”. These terms are undefined, and are interpreted in widely different ways by different stakeholders.

The definition of a traditional compounder in this legislation includes compounding limited amounts in anticipation of a prescription pursuant to State law, which by some assessments also permits compounding without a prescription (aka office stock or hospital supply) where allowed by States. While some States may limit office-stock compounding, others may not. This would allow TCs to manufacture unlimited quantities of medicines.

To ensure that State-licensed pharmacies operating as TCs do not become *de facto* unregulated manufacturers, clear limits on the amount of compounding permitted in anticipation or without a prescription should be established. To ensure clarity and enforceability, Congress should: (1) direct FDA to establish volume thresholds for compounding in anticipation of/without a prescription through regulation and (2) clarify that this is a uniform Federal standard not pursuant to State law.

Alternatively, if a clear Federal standard is not established, compounding in anticipation or without a prescription should be regulated by States. However, this would undermine the protections established through the FDCA and put patients at risk from drugs made by unregulated manufacturers.

KASEY K. THOMPSON, PHARM.D

Question. We intended, with this discussion draft, to preserve traditional pharmacy practice and compounding. However, we have received a number of comments indicating concern with the scope of compounding “in limited quantities” by traditional compounders. Can you please explain what you foresee as potential problems, if any, with this definition? How can the committee improve this language if it is a problem?

Answer. Compounding in limited quantities is likely more applicable to community pharmacies that are largely retail but may also provide some compounded preparations to a local physician office or nursing facility, or even a hospital. It could be challenging to define “limited” to fit all the various practice settings in which compounding is conducted.

In the hospital setting, this is more difficult as many medications administered in a hospital are compounded preparations, either prepared in-house or out-source. This may vary among hospitals with children’s hospitals engaging in a larger share of compounding given their patient type. It is important to note that medications administered to a patient are only done so pursuant to a physician order, however, some preparations may need to be made ahead of time, operating room medications for example need to be at the ready for a potential emergency situation.

Anticipatory compounding should not be limited to such a degree that it compromises an efficient and safe compounding process or causes patients to have to wait for their drugs. However, “limited quantities” may need a more specific definition for the retail or community pharmacy setting.

In the retail or community compounding pharmacy, anticipatory compounding may be based on historical compounding logs, dispensing records, or orders by physicians. Practitioners and inspectors need regulatory clarification on what historical prescription data will be required and how it will be used to determine quantities that can be compounded in advance. Otherwise, they won’t know when the line is crossed and enforcement may be inconsistent. For example, would doses or units compounded in advance be approximately equal to those dispensed in the previous 60, 90, or 120 days?

Hospitals, on the other hand, keep detailed records on patients and their episodes of care and can better predict what drugs and how many doses should be prepared in advance. The majority of compounding is compounded sterile preparations (CSPs), many of which are expensive or in scarce supply and have short beyond-use dates (BUDs). Because of these conditions, only quantities required for filling current orders and other doses the organization can reasonably assure will be administered before the BUD are compounded in advance.

For the committee’s consideration the following language may serve as a starting point in describing “limited quantities”:

“limited quantities shall be based upon historical demand from the previous year, the previous quarter and any documented increased anticipated demand. The Secretary shall issue draft guidance within 180 days of enactment and final guidance 1 year after enactment.”

[Whereupon, at 12:04 p.m., the hearing was adjourned.]

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